



# IN THE UNITED STATES PATENT AND TRADEMARK OFFICE (Case No. 02-325-A (400/047))

In the	Application of:	
	Pavco et al.	
		Examiner:
Serial	No.: 10/712,633	
		Group Art Unit:
<b>Filing</b>	Date: November 13, 2003	
		Confirmation No. 6362
For:	Nucleic Acid Based Modulation of Female	
	Penroductive Diseases and Conditions	

## **INFORMATION DISCLOSURE STATEMENT**

Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450

Dear Sir:

Pursuant to 37 C.F.R. Section 1.97 - 1.99, the Applicant wishes to make the following references of record in the above-identified application. This Information Disclosure Statement is in compliance with the continuing duty of candor as set forth in 37 C.F.R. Section 1.56. Copies of the cited references are enclosed. These references are also listed on the enclosed PTO Form 1449.

The Office has waived the requirement under 37 CFR 1.98 (a)(2)(i) for submitting a copy of each cited U.S. patent and each U.S. patent application publication for all U.S. national patent applications filed after June 30, 2003 and for all international applications that have entered the national stage under 35 USC § 371 after June 30, 2003. In accordance with this waiver, cited U.S. patents and U.S. patent application publications are not enclosed.

This statement is not a representation that the listed references have effective dates early enough to be "prior art" within the meaning of 35 U.S.C. Section 102 or Section 103.

Applicants do not believe any fee is due with this submission. If this belief is in error and the Patent Office determines that the fee prescribed in the relevant portion of 37 C.F.R. Section 1.97 is applicable, the undersigned attorney by his signature hereby authorizes any such fee to be debited from Deposit Account 13-2490.

## **U.S. PATENT APPLICATION DOCUMENTS**

- \* Pavco et al., U.S. Patent Application No. 08/584,040 filed January 11, 1996
- \* Usman et al., U.S. Patent Application No. 08/878,640 filed June 19, 1997
- \* Sullenger et al., U.S. Patent Application No. 09/205,520 filed December 3, 1998
- \* Beigelman et al., U.S. Patent Application No. 09/301,511 filed April 28, 1999
- \* Pavco et al., U.S. Patent Application No. 09/371,772 (now U.S. Patent No. 6,566,127) filed August 10, 1999
- \* Beigelman et al., U.S. Patent Application No. 09/476,387 filed December 30, 1999
- \* Pavco et al., U.S. Patent Application No. 09/708,690 filed November 7, 2000
- \* Pavco et al., U.S. Patent Application No. 09/870,161 filed May 29, 2001
- Usman et al., U.S. Patent Application No. 09/877,526 filed June 8, 2001
- Beigelman et al., U.S. Patent Application No. 09/918,728 filed July 31, 2001
- Pavco et al., U.S. Patent Application No. 10/138,674 filed May 3, 2002
- \* Pavco et al., U.S. Patent Application No. 60/005,974 filed October 26, 1995
- \* Thompson et al., U.S. Patent Application No. 60/082,404 filed April 20, 1998
- Hartmann et al., U.S. Patent Application No. 60/101,174 filed September 21, 1998
- \* Sandberg et al., U.S. Patent Application No. 60/334,461 filed November 30, 2001

## **U. S. PATENTS**

- \* Cech et al., U.S. Patent No. 4,987,071, issued January 22, 1991
- \* Gold et al., U.S. Patent No. 5,270,163, issued December 14, 1993
- \* Sproat et al., U.S. Patent No. 5,334,711, issued August 2, 1994
- \* Gold et al., U.S. Patent No. 5,475,096, issued December 12, 1995

- \* McSwiggen et al., U.S. Patent No. 5,525,468, issued June 11, 1996
- \* Shih et al., U.S. Patent No. 5,589,332, issued December 31, 1996
- \* Noonberg et al., U.S. Patent No. 5,624,803, issued April 29, 1997
- \* Chowrira et al., U.S. Patent No. 5,631,359, issued May 20, 1997
- \* Cook et al., U.S. Patent No. 5,670,633, issued September 23, 1997
- \* Usman et al., U.S. Patent No. 5,672,053, issued September 30, 1997
- \* Eckstein et al., U.S. Patent No. 5,672,695, issued September 30, 1997
- Beigelman et al., U.S. Patent No. 5,716,824, issued February 10, 1998
- \* George et al., U.S. Patent No. 5,741,679, issued April 21, 1998
- \* Buhr et al., U.S. Patent No. 5,792,847, issued August 11, 1998
- \* Joyce et al., U.S. Patent No. 5,807,718, issued September 15, 1998
- \* George et al., U.S. Patent No. 5,834,186, issued November 10, 1998
- Woolf or Arrow?? Et al., U.S. Patent No. 5,849,902, issued December 15, 1998
- \* Sullenger and Cech, U.S. Patent No. 5,854,038, issued December 29, 1998
- \* Nathan et al., U.S. Patent No. 5,871,914, issued February 16, 1999
- \* Crooke, U.S. Patent No. 5,898,031, issued April 27, 1999
- \* Arrow et al., U.S. Patent No. 5,989,912, issued November 23, 1999
- \* Brennan, U.S. Patent No. 6,001,311, issued December 14, 1999
- \* Cook et al., U.S. Patent No. 6,005,087, issued December 21, 1999
- \* Crooke, U.S. Patent No. 6,107,094, issued August 22, 2000
- \* Eckstein et al., U.S. Patent No. 6,127,173, issued October 3, 2000
- \* Usman et al., U.S. Patent No. 6,159,714, issued December 12, 2000
- \* Kaplitt et al., U.S. Patent No. 6,180,613, issued January 30, 2001
- Gold et al., U.S. Patent No. 6,300,074, issued October 9, 2001
- \* Buhr et al., U.S. Patent No. 6,476,205, issued November 5, 2002

## FOREIGN PATENT DOCUMENTS

- \* Hampel et al., European Patent No. 0 360 257, issued March 28, 1990
- \* Arnold et al., International Publication No. WO 89/02439, published April 23, 1989
- \* Rossi et al., International Publication No. WO 91/03162, published March 21, 1991

- \* Eckstein et al., International Publication No. WO 92/07065, published September 23, 1991
- \* Usman et al., International Publication No. WO 93/15187, published August 5, 1993
- \* Thompson et al., International Publication No. WO 93/23057, published November 25, 1993
- 1. Draper et al., International Publication No. WO 93/23569, published November 25, 1993
- Sullivan et al., International Publication No. WO 94/02595, published February 3, 1994
- \* Robinson, International Publication No. WO 95/04142, published February 9, 1995
- \* Draper et al., International Publication No. WO 95/04818, published February 16, 1995
- \* Usman et al., International Publication No. WO 95/06731, published March 9, 1995
- Usman et al., International Publication No. WO 95/11304, published April 27, 1995
- \* Dudycz et al., International Publication No. WO 95/11910, published May 4, 1995
- \* Draper et al., International Publication No. WO 95/13380, published May 18, 1995
- \* Rockwell et al., International Publication No. WO 95/21868, published August 17, 1995
- \* Stinchcomb et al., International Publication No. WO 95/23225, published August 31, 1995
- \* Asnell et al., International Publication No. WO 96/10390, published April 11, 1996
- \* Holland et al., International Publication No. WO 96/10391, published April 11, 1996
- \* Choi et al., International Publication No. WO 96/10392, published April 11, 1996
- 2. Beigelman et al., International Publication No. WO 96/18736, published June 20, 1996
- Pyle et al., International Publication No. WO 96/22689, published August 1, 1996
- 3. Pavco et al., International Publication No. WO 97/15662, published May 1, 1997
- \* Wincott et al., International Publication No. WO 97/26270, published July 4, 1997
- \* Woolf et al., International Publication No. WO 98/13526, published April 2, 1998
- \* Breaker et al., International Publication No. WO 98/27104, published June 25, 1998
- Karpeisky et al., International Publication No. WO 98/28317, published July 2, 1998.
- 4. Breaker et al., International Publication No. WO 98/43993, published March 30, 1998
- \* Ludwig et al., International Publication No. WO 98/58058, published December 23, 1998
- 5. Klimuk et al., International Publication No. WO 99/04819, published February 4, 1999
- 6. Beigelman et al., International Publication No. WO 99/05094, published February 4, 1999
- 7. Deschamps de Paillette et al., International Publication No. WO 99/07409, published February 18, 1999
- 8. Wengel et al., International Publication No. WO 99/14226, published September 14, 1999

- \* Eckstein et al., International Publication No. WO 99/16871, published April 8, 1999
- 9. Fire et al., International Publication No. WO 99/32619, published July 1, 1999
- 10. Graham et al., International Publication No. WO 99/49029, published September 30, 1999
- 11. Waterhouse et al., International Publication No. WO 99/53050, published October 21, 1999
- 12. Thomspon et al., International Publication No. WO 99/54459, published October 28, 1999
- \* Beigelman et al., International Publication No. WO 99/55857, published November 4, 1999
- 13. Heifitz et al., International Publication No. WO 99/61631, published December 2, 1999
- 14. Storella et al., International Publication No. WO 99/63116, published December 9, 1999
- 15. Plaetinck et al., International Publication No. WO 00/01846, published January 13, 2000
- Nathan et al., International Publication No. WO 00/24931, published May 4, 2000
- Breaker et al., International Publication No. WO 00/26226, published May 11, 2000
- 16. Kreutzer et al., International Publication No. WO 00/44895, published August 3, 2000
- 17. Li et al., International Publication No. WO 00/44914, published August 3, 2000
- 18. Pachuk et al., International Publication No. WO 00/63364, published October 26, 2000
- 19. Wengel et al., International Publication No. WO 00/66604, published May 4, 2000
- 20. Labarbera et al., International Publication No. WO 00/73416, published December 7, 2000
- 21. Mello and Fire, International Publication No. WO 01/29058, published April 26, 2001
- 22. Pappa, International Publication No. WO 01/32920, published May 10, 2001
- 23. Zernicka-Goetz et al., International Publication No. WO 01/36646, published May 25, 2001
- 24. Tuschl et al., International Publication No. WO 01/75164, published October 11, 2001
- 25. Escobedo, International Publication No. WO 02/096927 (PCT/US02/17674), published December 5. 2002

## **OTHER DOCUMENTS**

- \* Aiello et al., "Suppression of Retinal Neovascularization in vivo by Inhibition of Vascular Endothelial Growth Factor (VEGF) Using Soluble VEGF-Receptor Chimeric Proteins," <u>Proc. Natl. Acad. Sci. USA</u> 92: 10457-10461 (1995)
- \* Aiello, et al., "Vascular Endothelial Growth Factor in Ocular Fluid of Patients with Diabetic Retinopathy and Other Retinal Disorders," 1994 New Engl. J. Med. 331, 1480

- \* Akhtar and Juliano, "Cellular Uptake and Intracellular Fate of AntiSense Oligonucleotides," <u>Trends Cell Biol.</u> 2:139-144 (1992)
- 26. Aldrian-Herrada et al., "A peptide nucleic acid (PNA) is more rapidly internalized in cultured neurons when coupled to a *retro-inverso* delivery peptide. The antisense activity depresses the target mRNA and protein in magnocellular oxytocin neurons," <u>Nucleic Acids Research</u> 26:4910-4916 (1998)
- 27. Bahramian et al., "Transcriptional and Posttranscriptional Silencing of Rodent α1(I) Collagen by a Homologous Transcriptionally Self-Silenced Transgene," Molecular and Cellular Biology, 274-283 (1999)
- \* Bartel and Szostak, "Isolation of New Ribozymes From a Large Pool of Random Sequences," <u>Science</u> 261:1411-1418 (1993)
- 28. Bass, "The short answer," Nature 411:428-429 (2001)
- \* Beaucage and Iyer, "The Functionalization of Oligonucleotides Via Phosphoramidite Derivatives," <u>Tetrahedron</u> 49:1925-1963 (1993)
- 29. Beaudry and Joyce, "Directed Evolution of an RNA Enzyme," <u>Science</u> 257:635-641 (1992)
- \* Beigelman et al., "Chemical Modification of Hammerhead Ribozymes," <u>J. Biol. Chem.</u> 270:25702-25708 (1995)
- 30. Bellon et al., "Amino-Linked Ribozymes: Post-Synthetic Conjugation of Half-Ribozymes," *Nucleosides & Nucleotides* 16:951-954 (1997)
- 31. Bellon et al., "Post-synthetically Ligated Ribozymes: An Alternative Approach to Iterative Solid Phase Synthesis," <u>Bioconjugate Chem.</u> 8:204-212 (1997)
- 32. Berzal-Herranz et al., "Essential nucleotide sequences and secondary structure elements of the hairpin ribozyme," EMBO J. 12:2567-2574 (1993)
- 33. Blesch, "Delivery of Neurotrophic Factors to Neuronal Targets: Toward Gene Therapy in the CNS," <u>Drug News & Perspectives</u> 13:269-280 (2000)
- 34. Boado et al., "Drug Delivery of Antisense Molecules to the Brain for Treatment of Alzheimer's Disease and Cerebral AIDS," *Journal of Pharmaceutical Sciences* 87:1308-1315 (1998)
- 35. Boado, "Antisense drug delivery through the blood-brain barrier," *Advanced Drug Delivery Reviews* 15:73-107 (1995)

- \* Breaker and Joyce, "Inventing and improving ribozyme function: rational design versus iterative selection methods," <u>TIBTECH</u> 12:268-275 (1994)
- \* Breaker et al., "A DNA enzyme with Mg²-dependent RNA phosphoesterase activity," Chemistry & Biology 2(10):655-660 (1995)
- Breaker, "Are engineered proteins getting competition from RNA?" <u>Current</u>
   <u>Opinion in Biotechnology</u> 7:442-448 (1996)
- 36. Breaker, "Catalytic DNA: in training and seeking employment," *Nature Biotechnology* 17:422-423 (1999)
- 37. Brennan et al., "Two-Dimensional Parallel Array Technology as a New Approach to Automated Combinatorial Solid-Phase Organic Synthesis," *Biotechnology and Bioengineering (Combinatorial Chemistry)* 61:33-45 (1998)
- 38. Brody and Gold, "Aptamers as therapeutic and diagnostic agents," *Reviews in Molecular Biotechnology* 74:5-13 (2000)
- 39. Brogniez et al., "Fluorescence of Experimented Endometriosis in Rabbits, Using Tamoxifen-eosin Association," <u>Human Reproduction</u> 10:927-931 (1995)
- \* Burger et al., "Experimental Corneal Neovascularization: Biomicroscopic, Angiographic, and Morphologic Correlation," *Cornea* 4:35-41 (1985/1986)
- \* Burgin et al., "Chemically Modified Hammerhead Ribozymes with Improved Catalytic Rates," <u>Biochemistry</u> 35:14090-14097 (1996) (volume no mistakenly listed as 6)
- 40. Burlina et al., "Chemical Engineering of RNase Resistant and Catalytically Active Hammerhead Ribozymes," *Bioorganic & Medicinal Chemistry* 5:1999-2010 (1997)
- \* Caruthers et al., "Chemical Synthesis of Deoxyoligonucleotides and Deoxyoligonucleotide Analogs," <u>Methods in Enzymology</u> 211:3-19 (1992)
- \* Cech, "Ribozymes and Their Medical Implications," <u>JAMA</u> 260:3030-3034 (1988)
- \* Chartrand et al., "An oligodeoxyribonucleotide that supports catalytic activity in the hammerhead ribozyme domain," <u>Nucleic Acids Research</u> 23(20):4092-4096 (1995)

- \* Chen et al., "Multitarget-Ribozyme Directed to Cleave at up to Nine Highly Conserved HIV-1 env RNA Regions Inhibits HIV-1 Replication-Potential Effectiveness Against Most Presently Sequenced HIV-1 Isolates," <u>Nucleic Acids Research</u> 20:4581-4589 (1992)
- \* Chowrira et al., "In Vitro and in Vivo Comparison of Hammerhead, Hairpin, and Hepatitis Delta Virus Self-Processing Ribozyme Cassettes," <u>J. Biol. Chem.</u> 269:25856-25864 (1994)
- \* Christoffersen and Marr, "Riobozymes as Human Therapeutic Agents," <u>J. Med. Chem.</u> 38:2023-2037 (1995) (also referred to as Christofferson and Marr)
- 41. Christoffersen et al., "Application of computational techologies to ribozyme biotechnology products," <u>Journal of Molecular Structure (Theochem)</u> 311:273-284 (1994) (maybe referred to as Christofferson)
- \* Cload and Schepartz, "Polyether Tethered Oligonucleotide Probes," <u>J. Am. Chem. Soc.</u> 113:6324-6326 (1991)
- Collins and Olive, "Reaction Conditions and Kinetics of Self-Cleavage of a Ribozyme Derived From *Neurospora* VS RNA," <u>Biochemistry</u> 32:2795-2799 (1993)
- 42. Couture and Stinchcomb, "Anti-gene therapy: the use of ribozymes to inhibit gene function," Trends In Genetics 12:510-515 (1996)
- 43. Crooke, "Advances in Understanding the Pharmacological Properties of Antisense Oligonucleotides," Advances in Pharmacology 40:1-49 (1997)
- 44. Crooke, "Antisense Therapeutics," <u>Biotechnology and Genetic Engineering</u>
  <u>Reviews</u> 15:121-157 (1998)
- 45. Crooke, "Progress in Antisense Technology: The End of the Beginning," Methods in Enzymology 313:3-45 (1999)
- 46. Cummings and Metcalf, "Effect of Surgically Induced Endometriosis on Pregnancy and Effect of Pregnancy and Lactation on Endometriosis in Mice<sup>1</sup>" P.S.E.B.M. 212:332-337 (1996)
- 47. Cummings et al., "Promotion of Endometriosis by 2,3, 7, 8-Tetrachlorodibenzo-*p*-dioxin in Rats and Mice: Time-Dose Dependence and Species Comparison<sup>1,2</sup>" <u>Toxicology and Applied Pharmacology</u> 138:131-139 (1996)

- 48. D'Hooghe et al., "The Cycle Pregnancy Rate is Normal in Baboons with Stage I Endometriosis but Decreased in Primates with Stage II and Stage III-IV Disease," Fertility and Sterility 66:809-813 (1996)
- 49. Delihas et al., "Natural antisense RNA/target RNA interactions: Possible models for antisense oligonucleotide drug design," Nature Biotechnology 15:751-753 (1997)
- \* Detmar et al., "Overexpression of Vascular Permeability Factor/Vascular Endothelial Growth Factor and its Receptors in Psoriasisi," 1994 J. Exp. Med. 180, 1141
- 50. Donnez et al., "Vascular Endothelial Growth Factor (VEGF) in Endometriosis," <u>Human Reproduction</u> 13:1686-1690 (1998)
- \* Dreyfus, "Restriction Ribozymes?" <u>Einstein Quarterly Journal of Biology and Medicine</u> 6:92-93 (1988)
- \* Dropulic et al., "Functional Characterization of a U5 Ribozyme: Intracellular Suppression of Human Immunodeficiency Virus Type I Expression," <u>Journal</u> of Virology 66:1432-1441 (1992)
- \* Durand et al., "Circular Dichroism Studies of an Oligodeoxyribonucleotide Containing a Hairpin Loop Made of a Hexaethylene Glycol Chain: Conformation and Stability," Nucleic Acids Research 18:6353-6359 (1990)
- \* Duval-Valentin, "Specific inhibition of transcription by triple helix-forming oligonucleotides," <a href="Proc. Natl. Acad. Sci. USA">Proc. Natl. Acad. Sci. USA</a> 89:504-508 (1992)
- 51. Earnshaw et al., "Modified Oligoribonucleotides as Site-Specific Probes of RNA Structure and Function," *Biopolymers* 48:39-55 (1998)
- \* Egholm et al., "PNA hybridizes to complementary oligonucleotides obeying the Watson-Crick hydrogen-bonding rules," Nature 365:566-568 (1993)
- 52. Elbashir et al., "Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells," *Nature* 411:494-498 (2001)
- 53. Elkins and Rossi, "Ch. 2 Cellular Delivery of Ribozymes," in <u>Delivery Strategies for Antisense Oligonucleotide Therapeutics</u>, edited by Akhtar, CRC Press, pp. 17-220 (1995)
- Elroy-Stein and Moss, "Cytoplasmic Expression System Based on Constitutive Synthesis of Bacteriophage T7 RNA Polymerase in Mammalian Cells," <a href="Proc. Natl. Acad. Sci. USA">Proc. Natl. Acad. Sci. USA</a> 87:6743-6747 (1990)

- 54. Genbank Accession no. X51602
- 55. Emerich et al., "Biocompatability of Poly (DL-Lactide-co-Glycolide)
  Microshperes Implanted Into the Brain," Cell Transplantation 8:47-58 (1999)
- 56. Fasciani et al., "High Concentrations of the Vascular Endothelial Growth Factor and Interleukin-8 in Ovarian Endometriomata," Molecular Human Reproduction 6:50-54 (2000)
- \* Fava et al., "Vascular Permeability Factor/Endothelial Growth Factor (VPF/VEGF): Accumulation and Expression in Human Synovial Fluids and Rheumatoid Synovial Tissue," 1994 J. Exp. Med. 180, 341
- \* Feldstein et al., "Two sequences participating in the autolytic processing of satellite tobacco ringspot virus complementary RNA," <u>Gene</u> 82:53-61 (1989)
- \* Ferentz and Verdine, "Disulfied Cross-Linked Oligonucleotides," <u>J. Am. Chem. Soc.</u> 113:4000-4002 (1991)
- Ferrara, "Vascular Endothelial Growth Factor," 1993 Trends Cardiovas. Med.
   3, 2244
- 57. Fire et al., "Potent and Specific Genetic Interference by Double-Stranded RNA in Caenorhabditis Elegans," Nature 391:806-811(1998)
- \* Folkman and Shing, "Angiogenesis," <u>J. Biol. Chem.</u> 267:10931-10934 (1992)
- 58. Folkman et al., "Long-term Culture of Capillary Endothelial Cells," <u>Proc. Natl.</u> Acad. Sci. USA 76:5217-5221 (1979)
- \* Folkman, "What is the Evidence that Tumors are Angiogenesis Dependent?" Journal of the National Cancer Institute 82:4-6 (1990)
- \* Folkman, "Tumor Agniogenesis" 1985 Adv. Cancer. Res. 43, 175
- \* Fong et al., "Role of the Flt-1 Receptor Tyrosine Kinase in Regulating the Assembly of Vascular Endothelium," 1995 Nature 376, 66 Corrected from specification
- Forster and Altman, "External Guide Sequences for an RNA Enzyme,"
   Science 249:783-786 (1990)
- 59. Fox, "Targeting DNA with Triplexes," *Current Medicinal Chemistry* 7:17-37 (2000)

- \* Freier et al., "Improved free-energy parameters for predictions of RNA duplex stability," <a href="Proc. Natl. Acad. Sci. USA">Proc. Natl. Acad. Sci. USA</a> 83:9373-9377 (1986) [sometimes referred to as Frier]
- \* Gao and Huang, "Cytoplasmic Expression of a Reporter Gene by Co-Delivery of T7 RNA Polymerase and T7 Promoter Sequence with Cationic Liposomes," Nucleic Acids Research 21:2867-2872 (1993)
- 60. Genbank Accession No. NM 002019
- 61. Genbank Accession No. NM\_002253
- 62. Genbank Accession No. NM 003376
- \* Gitay-Goren *et al.*, "The Binding of Vascular Endothelial Growth Factor to Its Receptos is Dependent on Cell Surface-associated Heparin-like Molecules," 1992 *J. Biol. Chem.* 267, 6093
- \* Gold et al., Diversity of Oligonucleotide Functions," <u>Annu. Rev. Biochem.</u> 64:763-797 (1995)
- 63. Gold, "Axonal Regeneration of Sensory Nerves is Delayed by Continuous Intrathecal Infusion of Nerve Growth Factor," *Neuroscience* 76:1153-1158 (1997)
- 64. Good et al., "Expression of small, therapuetic RNAs in human nuclei," <u>Gene Therapy</u> 4:45-54 (1997)
- \* Grant et al., "Insulin-like growth factor I acts as an angiogenic agent in rabbit cornea and retina: comparative studies with basic fibroblast growth factor," *Diabetologia* 36:282-291 (1993)
- \* Griffin et al., "Group II intron ribozymes that cleave DNA and RNA linkages with similar efficiency, and lack contacts with substrate 2'-hydroxyl groups," <u>Chemistry & Biology</u> 2:761-770 (1995)
- 65. Groothuis and Levy, "The entry of antiviral and antiretroviral drugs into the central nervous system," <u>Journal of NeuroVirology</u> 3:387-400 (1997)
- \* Guerrier-Takada et al., "The RNA Moiety of Ribonuclease P Is the Catalytic Subunit of the Enzyme," Cell 35:849-857 (1983)
- 66. Guo and Collins, "Efficent *trans*-cleavage of a stem-loop RNA substrate by a ribozyme derived from *Neurospora* VS RNA," <u>EMBO J.</u> 14:368-376 (1995)

- Hagihara et al., "Widespread gene transfection into the central nervous system of primates," Gene Therapy 7:759-763 (2000)
- 68. Hamilton, et al., "A Species of Small Antisense RNA in Posttranscriptional Gene Silencing in Plants," *Science*, 286, 950-952 (1999)
- 69. Hammann et al., "Length Variation of Helix III in a Hammerhead Ribozyme and Its Influence on Cleavage Activity," *Antisense & Nucleic Acid Drug Development* 9:25-31 (1999)
- \* Hampel and Tritz, "RNA Catalytic Properties of the Minimum (-)sTRSV Sequence," <u>Biochemistry</u> 28:4929-4933 (1989)
- \* Hampel et al., "'Hairpin' Catalytic RNA Model: Evidence for Helices and Sequence Requirement for Substrate RNA," <u>Nucleic Acids Research</u> 18:299-304 (1990)
- \* Haseloff and Gerlach, "Sequences required for self-catalysed cleavage of the satellite RNA of tobacco ringspot virus," <u>Gene</u> 82:43-52 (1989)
- \* Haseloff and Gerlach, "Simple RNA Enzymes with New and Highly Specific Endoribonuclease Activities," Nature 334:585-591 (1988)
- 70. Hermann and Patel, "Adaptive Recognition by Nucleic Acid Aptamers," *Science* 287:820-825 (2000)
- 71. Herrlinger et al., "HSV-1 Vectors for Gene Therapy of Experimental CNS Tumors," Methods Mol. Med. 35:287-312 (2000)
- \* Hertel et al., "Numbering System for the Hammerhead," <u>Nucleic Acids</u> <u>Research</u> 20:3252 (1992)
- 72. Ho et al., "Antisense Oligonucleotides for Target Validation in the CNS," <u>Current Opinion in Molecular Therapeutics</u> 1:336-343 (1999)
- 73. Hunziker et al., "Nucleic Acid Analogues: Synthesis and Properties, in Modern Synthetic Methods," VCH, 331-417 (1995)
- \* Ishiwata et al., "Physical-Chemistry Characteristics and Biodistribution of Poly(ethylene glycol)-Coated Liposomes Using Poly(oxyethylene) Cholesteryl Ether," Chem. Pharm. Bull. 43:1005-1011 (1995) (mistakenly referred to as Ishiwataet)
- Ishizaka et al., "Isolation of Active Ribozymes from an RNA Pool of Random Sequences Using an Anchored Substrate RNA," <u>Biochemical and Biophysical</u> <u>Research Communication</u> 214(2):403-409 (1995)

- Izant and Weintraub, "Constitutive and Conditional Suppression of Exogenous and Endogeneous Genes by Anti-Sense RNA," <u>Science</u> 229:345-352 (1985)
- \* Jaeger et al., "Improved Predictions of Secondary Structures for RNA," <u>Proc.</u>
  Natl. Acad. Sci. USA 86:7706-7710 (1989)
- 74. Jarvis et al., "Optimizing the Cell Efficacy of Synthetic Ribozymes," <u>Journal of Biological Chemistry</u> 271:29107-29112 (1996)
- \* Jaschke et al., "Automated Incorporation of Polyethylene Glycol into Synthetic Oligonucleotides," Tetrahedron Letters 34:301-304 (1993)
- 75. Jayasena, "Aptamers: An Emerging Class of Molecules that Rival Antibodies in Diagnostics," *Clinical Chemistry* 45:1628-1650 (1999)
- \* Jeffries and Symons, "A Catalytic 13-mer Ribozyme," <u>Nucleic Acids</u> <u>Research</u> 17:1371-1377 (1989) (also referred to as Jefferies)
- Jellinek et al., "Inhibitions of Receptor Binding by High-Affinity RNA Ligands to Vascular Endothelial Growth Factor," <u>Biochemistry</u> 33:10450-10456 (1994)
- 76. Jolliet-Riant and Tillement, "Drug transfer across the blood-brain barrier and improvement of brain delivery," *Fundam. Clin. Pharmacol.* 13:16-26 (1999)
- \* Joyce et al., "Amplification, mutation and selection of catalytic RNA," <u>Gene</u> 82:83-87 (1989)
- \* Joyce, "Directed Molecular Evolution," <u>Scientific American</u> 267:90-97 (1992)
- 77. Karpeisky et al, "Highly Efficient Synthesis of 2'-O-Amino Nucleosides And Their Incorporation in Hammerhead Ribozymes," <u>Tetrahedron Letters</u> 39:1131-1134 (1998)
- Kashani-Sabet et al., "Reversal of the Malignant Phenotype by an Anti-ras Ribozyme," <u>Antisense Research & Development</u> 2:3-15 (1992)
- \* Kim and Cech, "Three-dimensional model of the active site of the self-splicing rRNA precursor of *Tetrahymena*," <u>Proc. Natl. Acad. Sci. USA</u> 84:8788-8792 (1987)
- Kim et al., "Inhibition of vascular endothelial growth factor-induced angiogenesis suppresses tumour growth in vivo," Nature 362:841-844 (1993)

- \* Koch *et al.*, "Vascular Endothelial Growth Factor: A Cytokine Modulating Endothelial Function in Rheumatoid Arthritis," 1994 *J. Immunol.* 152, 4149
- \* Kore, et al., "Sequence specificity of the hammerhead ribozyme revisistsed; the NIH rule", <u>Nucleic Acids Research</u>, 26(18):4116-4120 (1998).
- \* Kumar and Ellington, "Artificial evolution and natural ribozymes," <u>FASEB J.</u> 9:1183-1195 (1995)
- 78. Kusser, "Chemically modified nucleic acid aptamers for in vitro selections: evolving evolution," *Reviews in Molecular Biotechnology* 74:27-38 (2000)
- Lasic and Needham "The 'Stealth' Liposome: A Prototypical Biomaterial,"
   Chemical Reviews 95:2601-2627 (1995)
- 79. Lasic and Papahadjopoulos, "Liposomes Revisited," <u>Science</u> 267:1275-1276 (1995)
- \* Lepri et al., "Effect of Low Molecular Weight Heparan Sulphate on Angiogenesis in the Rat Cornea after Chemical Cauterization," *Journal of Ocular Pharmacology* 10:273-281 (1994)
- \* L'Huillier et al., "Cytoplasmic Delivery of Ribozymes Leads to Efficient Reduction in  $\alpha$ -Lactalbumin mRNA Levels in C1271 Mouse," <u>EMBO J.</u> 11:4411-4418 (1992)
- \* Li and Altman, "Cleavage by RNase P of gene N mRNA reduces bacteriophage λ burst size," <u>Nucleic Acids Research</u> 24:835-842 (1996)
- \* Lieber et al., "Stable High-Level Gene Expression in Mammalian Cells by T7 Phage RNA Polymerase," <u>Methods Enzymol</u>. 217:47-66 (1993)
- \* Limbach et al., "Summary: the modified nucleosides of RNA," <u>Nucleic Acids</u> Research 22(12):2183-2196 (1994)
- 80. Lin and Matteucci, "A Cytosine Analogue Capable of Clamp-Like Binding to a Guanine in Helical Nucleic Acid," *J. Am. Chem. Soc.* 120:8531-8532 (1998)
- 81. Lin et al., "Policing rogue genes," Nature, 402, 128-129 (1999)
- \* Lisziewicz et al., "Inhibition of Human Immunodeficiency Virus Type 1 Replication by Regulated Expression of a Polymeric Tat Activation Response RNA Decoy as a Strategy for Gene Therapy in AIDS," <u>Proc. Natl. Acad. Sci.</u> <u>U.S.A.</u> 90:8000-8004 (1993)

- \* Liu et al., "Cationic Liposome-mediated Intravenous Gene Delivery," <u>J. Biol. Chem.</u> 270(42):24864-24870 (1995)
- Long and Uhlenbeck, "Kinetic characterization of intramolecular and intermolecular hammerhead RNAs with stem II deletions," <u>Proc. Natl. Acad.</u> <u>Sci. USA</u> 91:6977-6981 (1994)
- \* Ma et al., "Design and Synthesis of RNA Miniduplexes via a Synthetic Linker Approach," <u>Biochemistry</u> 32:1751-1758 (1993)
- \* Ma et al., "Design and Synthesis of RNA Miniduplexes via a Synthetic Linker Approach. 2. Generation of Covalently Closed, Double-Stranded Cyclic HIV-1 TAR RNA Analogs with High Tat-Binding Affinity," <u>Nucleic Acids Research</u> 21:2585-2589 (1993)
- 82. Maher et al., "Kinetic Analysis of Oligodeoxyribonucleotide-Directed Triple-Helix Formation on DNA," *Biochemistry* 29:8820-8826 (1990)
- \* Mathews et al., "A Receptor Tyrosine Kinase cDNA Isolated from a Population of Enriched Primitive Hematopoiectic cells and Exhibiting Close Genetic Linkage to c-kit," 1991, Proc. Natl. Acad. Sci., USA, 88, 9026
- \* McCurdy et al., "Deoxyoligonucleotides with Inverted Polarity: Synthesis and Use in Triple-Helix Formation" <u>Nucleosides & Nucleotides</u> 10:287-290 (1991)
- \* McGarry and Lindquist, "Inhibition of heat shock protein synthesis by heat-inducible antisense RNA," <a href="Proc. Natl. Acad. Sci. USA">Proc. Natl. Acad. Sci. USA</a> 83:399-403 (1986)
- 83. McLaren et al., "Vascular Endothelial Growth Factor (VEGF) Concentrations are Elevated in Peritoneal Fluid of Women with Endometriosis," <u>Human Reproduction</u> 11:220-223 (1996)
- 84. McLaren et al., "Vascular Endothelial Growth Factor is Produced by Peritoneal Fluid Macrophages in Endometriosis and Is Regulated by Ovarian Steroids," J. Clin. Invest. 98:482-489 (1996)
- 85. McLaren, "Vascular Endothelial Growth Factor and Endometriotic Angiogenesis," <u>Human Reproduction Update</u> 6:45-55 (2000)
- 86. Mesmaeker et al, "Novel Backbone Replacements for Oligonucleotides," American Chemical Society, pp. 24-39 (1994)
- \* Michels and Pyle, "Conversion of a Group II Intron into a New Multiple-Turnover Ribozyme that Selectively Cleaves Oligonucleotides: Elucidation of Reaction Mechanism and Structure/Function Relationships," <u>Biochemistry</u> 34:2965-2977 (1995)

- 87. Millauer et al., "Glioblastoma growth inhibited *in vivo* by a dominant-negative Flk-1 mutant," *Letters to Nature* 367:576-579 (1994)
- Millauer, "High Affintiy VEGF Binding and Developmental Expression Suggest Flk-1 as a Major Regulator of Vasculogenesis and Angiogenesis," Cell 72:835-846 (1993)
- \* Miller et al., "Vascular Endothelial Growth Factor/Vascular Permeability Factor is Temporally and Spatially Correlated with Ocular Angiogenesis in a Primate Model," 1994 Am. J. Pathol. 145, 574
- 88. Milligan and Uhlenbeck, "Synthesis of Small RNAs Using T7 RNA Polymerase," <u>Methods Enzymol.</u> 180:51-62 (1989)
- 89. Milner et al., "Selecting effective antisense reagents on combinatorial oligonucleotide arrays," *Nature Biotechnology* 15:537-541 (1997)
- 90. Moore and Sharp, "Site-Specific Modification of Pre-mRNA: The 2'-Hydroxyl Groups at the Splice Sites," <u>Science</u> 256:992-996 (1992)
- \* Mukhopadhyay et al., "Antisense Regulation of Oncogenes in Human Cancer," <u>Critical Reviews in Oncogenesis</u> 7:151-190 (1996)
- Nakamaye and Eckstein, "AUA-Cleaving Hammerhead Ribozymes: Attempted Selection for Improved Cleavage," <u>Biochemistry</u> 33:1271-1277 (1994)
- \* Nathans and Smith, "Restriction Endonucleases in the Analysis and Restructuring of DNA Molecules," <u>Ann. Rev. Biochem.</u> 44:273-293 (1975)
- \* Neufeld et al., "Vascular Endothelial Growth Factor and Its Receptors," Progress in Growth Factor Research 5:89-97 (1994)
- 91. Noonberg et al., *In vivo* generation of highly abundant sequence-specific oligonucleotides for antisense and triplex gene regulation," <u>Nucleic Acids Research</u> 22(14):2830-2836 (1994)
- \* Norrby, "Angiogenesis: new aspects relating to its initiation and control," *APMIA* 105:417-437 (1997)
- \* Ohkawa et al., "Activities of HIV-RNA Targeted Ribozymes Transcribed From a 'Shot-Gun' Type Ribozyme-trimming Plasmid," <u>Nucleic Acids Symp. Ser.</u> 27:15-16 (1992)

- Ojwang et al., "Inhibition of Human Immunodeficiency Virus Type 1
   Expression by a Hairpin Ribozyme," <u>Proc. Natl. Acad. Sci. USA</u> 89:10802-10806 (1992)
- \* Oku et al., "Real-time analysis of liposomal trafficking in tumor-bearing mice by use of positron emission tomography," <u>Biochimica et Biophysica Acta</u> 1238:86-90 (1995)
- \* Ono et al., "DNA Triplex Formation of Oligonucleotide Analogues Consisting of Linker Groups and Octamer Segments That Have Opposite Sugar-Phosphate Backbone Polarities," <u>Biochemistry</u> 30:9914-9921 (1991)
- O'Reilly et al., "Angiostatin: A Novel Angiogenesis Inhibitor That Mediates the Suppression of Metastases by a Lewis Lung Carcinoma," <u>Cell</u> 79:315-328 (1994)
- \* Orgel, "Selection in vitro," Proc. R. Soc. London B. 205:435-442 (1979)
- \* Ormerod et al., "Effects of Altering the Eicosanoid Precursor Pool on Neovascularization and Inflammation in the Alkali-burned Rabbit Cornea," American Journal of Pathology 137:1243-1252 (1990)
- \* Pandey et al., "Role ov B61, the Ligand for the Eck Receptor Tyrosine Kinase, in TNF-α-Induced Angiogenesis," *Science* 268:567-569 (1995)
- 92. Pardridge et al., "Vector-mediated delivery of a polyamide ("peptide") nucleic acid analogue through the blood-brain barrier *in vivo*," *Proc. Natl. Acad. Sci. USA* 92:5592-5596 (1995)
- Passaniti et al., "A Simple, Quantitative Method for Assessing Angiogenesis and Antiangiogenic Agents Using Reconstituted Basement Membrane, Heparin, and Fibroblast Growth Factor," *Laboratory Investigation* 67:519-528 (1992)
- 93. Peel and Klein, "Adeno-associated virus vectors: activity and applications in the CNS," <u>Journal of Neuroscience Methods</u> 98:95-104 (2000)
- \* Perreault et al., "Mixed Deoxyribo- and Ribo-Oligonucleotides with Catalytic Activity," Nature 344:565-567 (1990) (often mistakenly listed as Perrault)
- \* Perrotta and Been, "Cleavage of Oligoribonucleotides by a Ribozyme Derived from the Hepatitis δ Virus RNA Sequence," <u>Biochemistry</u> 31:16-21 (1992)
- 94. Peterson et al., "Future Prospects of Gene Therapy for Treating CNS Diseases," Central Nervous System Diseases Chapter 24:485-508 (2000)

- Pieken et al., "Kinetic Characterization of Ribonuclease-Resistant 2'-Modified Hammerhead Ribozymes," <u>Science</u> 253:314-317 (1991)
- 95. Pierce et al., "Regulation of Vascular Endothelial Growth Factor by Oxygen in a Model of Retinopathy of Prematurity," <u>Arch Ophthalmol</u> 114:1219-1228 (1996)
- \* Pierce et al., "Vascular endothelial growth factor/vascular permeability factor expression in a mouse model of retinal neovascularization," *Proc. Natl. Acad. Sci. USA* 92:905-909 (1995)
- 96. Plate, "Vascular endothelial growth factor is potential tumor angiogenesis factor in human gilomas *in vivo*," <u>Nature</u> 359:845-848 (1992)
- 97. Player and Torrence, "The 2-5A System: Modulation of Viral and Cellular Processes Through Acceleration of RNA Degradation," *Pharmacol Ther.* 78:55-113 (1998)
- \* Plouet et al., "Isolation and Characterization of a Newly Identified Endothelial Cell Mitogen Produced by AtT-20 Cells," EMBO J. 8, 3801 (1989)
- 98. Praseuth et al., "Triple helix formation and the antigene for sequence-specific control of gene expression," *Biochimica et Biophysica Acta* 1489:181-206 (1999)
- 99. Quereda et al., "Individual and Combined Effects of Triptoreline and Gestrinone on Experimental Endometriosis in Rats," <u>European Obstetrics & Gynecology and Reproductive Biology</u> 67:35-40 (1996)
- Richardson and Schepartz, "Tethered Oligonucleotide Probes. A Strategy for the Recognition of Structured RNA," <u>J. Am. Chem. Soc.</u> 113:5109-5111 (1991)
- \* Robinson et al., "Oligodeozynucleotides Inhibit Retinal Neovascularization in a Murine Model of Proliferation Retinopathy," <u>Proc. Natl. Acad. Sci. USA 93: 4851-4856 (1996)</u>
- \* Rossi et al., "Ribozymes as Anti-HIV-1 Therapeutic Agents: Principles, Applications, and Problems," <u>Aids Research and Human Retroviruses</u> 8:183-189 (1992)
- \* Santoro and Joyce, "A general purpose RNA-cleaving DNA enzyme," <u>Proc. Natl. Acad. Sci. USA</u> 94:4262-4266 (1997)

- 100. Santoro et al., "Mechanism and Utility of an RNA-Cleaving DNA Enzyme," Biochemistry 37:13330-13342 (1998)
- 101. Santoro et al., "RNA Cleavage by a DNA Enzyme with Extended Chemical Functionality," *J. Am. Chem. Soc.* 122:2433-2439 (2000)
  - \* Sarver et al., "Ribozymes as Potential Anti-HIV-1 Therapeutic Agents" Science 247:1222-1225 (1990)
  - Saville and Collins, "A Site-Specific Self-Cleavage Reaction Performed by a Novel RNA In Neurospora Mitochondria," <u>Cell</u> 61:685-696 (1990)
  - \* Saville and Collins, "RNA-Mediated Ligation of Self-Cleavage Products of a Neurospora Mitochondrial Plasmid Transcript," <u>Proc. Natl. Acad. Sci. USA</u> 88:8826-8830 (1991)
  - \* Scanlon et al., "Ribozyme-Mediated Cleavage of c-fos mRNA Reduces Gene Expression of DNA Synthesis Enzymes and Metallothionein," <a href="Proc. Natl.Acad. Sci. USA">Proc. Natl.Acad. Sci. USA</a> 88:10591-10595 (1991)
  - \* Scaringe et al., "Chemical synthesis of biologically active oligoribonucleotides using β-cyanoethyl protected ribonucleoside phosphoramidites," <u>Nucl Acids Res.</u> 18:5433-5441 (1990)
- 102. Schmajuk et al., "Antisense Oligonucleotides with Different Backbones," *The Journal of Biological Chemistry* 274:21783-21789 (1999)
- 103. Schroeder et al., "Diffusion Enhancement of Drugs by Loaded Nanoparticles in Vitro," *Prog. Neuro-Psychopharmacol. & Biol. Psychiat.* 23:941-949 (1999) [sometimes cited by RPI as *Prog Neuropsychopharmacol Biol Psychiatry* 23:941-949, 1999]
  - \* Seela and Kaiser, "Oligodeoxyribonucleotides containing 1,3-propanediol as nucleoside substitute," <u>Nucleic Acids Research</u> 15:3113-3129 (1987)
  - \* Senger et al., "Vascular permeability factor (VPF, VEGF) in tumor biology," Cancer and Matastasis Reviews 12:303-324 (1993)
- 104. Shabarova et al., "Chemical ligation of DNA: The first non-enyzmatic assembly of a biologically active gene," <u>Nucleic Acids Research</u> 19:4247-4251 (1991)
  - Shalaby *et al.*, "Failure of Blood-island Formation and Vasculogenesis in Flk-1-deficient Mice," 1995 *Nature* 376, 62

- 106. Sharkey et al., "Vascular Endothelial Growth Factor Expression in Human Endometrium is Regulated by Hypoxia," <u>The Journal of Clinical Endocrinology & Metabolism</u> 85:402-409 (2000)
- 107. Sharp et al., "RNAi and double-strand RNA," Genes & Development, 13:139-141 (1999)
- 108. Shibuya et al., "Nucleotide sequence and expression of a novel human receptor-type tyrosine kinase gene (flt) closely related to the fms family," Oncogene 5:519-524 (1990)
- 109. Shifren et al., "Ovarian Steroid Regulation of Vascular Endothelial Growth Factor in the Human Endometrium: Implications for Angiogenesis during the Menstrual Cycle and in the Pathogenesis of Endometriosis," The Journal of Clinical Endocrinology & Metabolism 81:3112-3118 (1996)
  - \* Shweiki et al., "Patterns of Expression of Vascular Endothelial Growth Factor (VEGF) and VEGF Receptors in Mice Suggest a Role in Hormonally Regulated Angiogenesis," 1993 Clin. Invest. 91: 2235-2243
- 110. Silverman et al., "Selective RNA Cleavage by Isolated RNase L Activated with 2-5A Antisense Chimeric Oligonucleotides," *Methods in Enzymology* 313:522-533 (1999)
  - \* Stein and Cheng, "Antisense Oligonucleotides as Therapeutic Agents Is the Bullet Really Magical?" <u>Science</u> 261:1004-1288 (1993)
- Stein et al., "A Specificity Comparison of Four Antisense Types: Morpholino, 2'-O-Methyl RNA, DNA, and Phosphorothioate DNA," <u>Antisense & Nucleic Acid Drug Development</u> 7:151-157 (1997)
- 112. Stoeckemann et al., "Effects of the Progesterone Antagonists Onapristone (ZK 98 299) and ZK 136 799 on Surgically Induced Endometriosis in Intact Rats," <u>Human Reproduction</u> 10:3264-3271 (1995)
- 113. Strauss, Evelyn, "Molecular Biology: Candidate 'Gene Silencers' Found," Molecular Biology, Vol. 286, No. 5441, p. 886 (1999) [sometimes mistakenly referred to as being published in Science]
- 114. Strobel and Dervan, "Site-Specific Cleavage of a Yeast Chromosome by Oligonucleotide-Directed Triple-Helix Formation," *Science* 249:73-75 (1990)
- 115. Sullenger et al., "Overexpression of TAR Sequences Renders Cells Resistant to Human Immunodeficiency Virus Replication," <u>Cell</u> 63:601-608 (1990)

- 116. Sun, "Technology evaluation: SELEX, Giliad Sciences Inc," <u>Current Opinion in Molecular Therapeutics</u> 2:100-105 (2000)
  - Szostak and Ellington, "Ch. 20 In Vitro Selection of Functional RNA Sequences," in <u>The RNA World</u>, edited by Gesteland and Atkins, Cold Spring Harbor Laboratory Press, pp. 511-533 (1993)
  - \* Szostak, "In Vitro Genes," TIBS 17:89-93 (1993)
  - \* Taira et al., "Construction of a novel RNA-transcript-trimming plasmid which can be used both *in vitro* in place of run-off and (G)-free transcriptions and *in vivo* as multi-sequences transcription vectors," <u>Nucleic Acids Research</u> 19:5125-5130 (1991)
  - \* Takahashi et al., "Markedly Increased Amounts of Messenger RNAs for Vascular Endothelial Growth Factor and Placenta Growth Factor in Renal Cell Carcinoma Associated with Angiogenesis," Cancer Research 54:4233-4237 (1994)
  - \* Takeshita *et al.*, "Therapeutic Angiogenesis: A Single Intraarterial Blous of Vascular Endothelial Growth Factor Augments Revascularization in a Rabbit Ischemic Hind Limb Model," 1995 *J. Clin. Invest.* 93, 662 **Corrected from Specification**
  - \* Tang et al., "Examination of the catalytic fitness of the hammerhead ribozyme by in vitor selection," RNA 3:914-925 (1997)
  - \* Terman et al., "Identification of a New Endothelial Cell Growth Factor Receptor Tyrosine Kinase," Oncogene 6, 1677 (1991)
  - \* Thompson et al., "Improved accumulation and activity of ribozymes expressed from a tRNA-based RNA polymerase III promoter," <u>Nucleic Acids Research</u> 23:2259-2268 (1995)
  - \* Torrence et al., "Targeting RNA for degradation with a (2'-5') oligoadenylate-antisense chimera," <a href="Proc. Natl. Acad. Sci. USA">Proc. Natl. Acad. Sci. USA</a> 90:1300-1304 (1993)
  - \* Turner et al., "Free Energy Increments for Hydrogen Bonds in Nucleic Acid Base Pairs," <u>J. Am. Chem. Soc.</u> 109:3783-3785 (1987)
  - \* Turner et al., "Improved Parameters for Prediction of RNA Structure," <u>Cold Spring Harbor Symposia on Quantitative Biology</u> Volume LII, pp. 123-133 (1987)

- 117. Tuschl et al., "Targeted mRNA Degradation by Double-Stranded RNA In Vitro," Genes & Development 13:3191-3197 (1999)
- 118. Tyler et al., "Peptide nucleic acids targeted to the neurotensin receptor and administered i.p. cross the blood-brain barrier and specifically reduce gene expression," Proc. Natl. Acad. Sci. USA 96:7053-7058 (1999)
- 119. Tyler et al., "Specific gene blockade shows that peptide nucleic acids readily enter neuronal cells in vivo," *FEBS Letters* 421:280-284 (1998)
  - \* Uhlenbeck, "A Small Catalytic Oligoribonucleotide," <u>Nature</u> 328:596-600 (1987)
- 120. Uhlmann and Peyman, "Antisense Oligonucleotides: A New Therapeutic Principle," <u>Chemical Reviews</u> 90:544-584 (1990)
  - \* Usman and Cedergren, "Exploiting the chemical synthesis of RNA," <u>TIBS</u> 17:334-339 (1992) (Corrected from Specification)
  - Usman and McSwiggen, "Ch. 30 Catalytic RNA (Ribozymes) as Drugs,"
     Annual Reports in Medicinal Chemistry 30:285-294 (1995)
  - \* Usman et al., "Automated Chemical Synthesis of Long Oligoribonucleotides Using 2'-O-Silylated Ribonucleoside 3'-O-Phosphoramidites on a Controlled-Pore Glass Support: Synthesis of a 43-Nucleotide Sequence Similar to the 3'-Half Molecule of an *Escherichia coli* Formylmethoionine tRNA," <u>J. Am.</u> <u>Chem. Soc.</u> 109:7845-7854 (1987)
  - \* Usman et al., "Chemical modification of hammerhead ribozymes: activity and nuclease resistance," <u>Nucleic Acids Syposium Series</u> 31:163-164 (1994)
- 121. Usman et al., "Hammerhead ribozyme engineering," <u>Current Opinion in Structural Biology</u> 1:527-533(1996)
  - \* Vaish et al., "Isolation of Hammerhead Ribozymes with Altered Core Sequences by *in Vitro* Selection," <u>Biochemistry</u> 36:6495-6501 (1997)
  - \* Vaisman *et al.*, "Characterization of the Receptors for Vascular Endothelial Growth," 1990 *J. Biol. Chem.*265, 19461
  - Ventura et al., "Activation of HIV-Specific Ribozyme Activity by Self-Cleavage," <u>Nucleic Acids Research</u> 21:3249-3255 (1993)
- 122. Verma and Eckstein, "Modified Oligonucleotides: Synthesis and Strategy for Users," *Annu. Rev. Biochem.* 67:99-134 (1998)

- 123. Warashina, et al., "Extremely High and Specific Activity of DNA Enzymes in Cells with a Philadelphia Chromosome, Chemistry & Biology, 6(4):237-250 (1999)
- 124. Waterhouse et al., "Virus resistance and gene silencing in plants can be induced by simultaneous expression of sense and antisense RNA," Proc. Natl. Acad. Sci. USA, 95, 13959-13964 (1998)
  - \* Weckbecker et al., 1992, Angiogenesis: Key principles-Science-Technology-Medicine, ed R. Steiner)
  - \* Weerasinghe et al., "Resistance to Human Immunodeficiency Virus Type 1 (HIV-1) Infection in Human CD4<sup>+</sup> Lymphocyte-Derived Cell Lines Conferred by Using Retroviral Vectors Expressing an HIV-1 RNA-Specific Ribozyme," Journal of Virology 65:5531-5534 (1994)
- 125. Wellstein and Czubayko, "Inhibition of Fibroblast Growth Factors," <u>Breast Cancer Research and Treatment</u> 38:109-119 (1996)
- 126. Werner and Uhlenbeck, "The effect of base mismatches in the substrate recognition helices of hammerhead ribozymes on binding and catalysis," <u>Nucleic Acids Research</u> 23:2092-2096 (1995)
  - Wincott et al., "Synthesis, deprotection, analysis and purification of RNA and ribozymes," <u>Nucleic Acids Research</u> 23(14):2677-2684 (1995)
- 127. Wincott et al., "A Practical Method for the Production of RNA and Ribozymes," Methods in Molecular Biology 74:59-69 (1997)
- 128. Woolf et al., "Specificity of Antisense Oligonucleotides *in vivo*," <u>Proc. Natl.</u> Acad. Sci. USA 89:7305-7309 (1992)
- Wu-Pong, "Oligonucleotides: Opportunities for Drug Therapy and Research," <u>BioPharm</u> pp20-33 (1994)
  - \* Yu et al., "A Hairpin Ribozyme Inhibits Expression of Diverse Strains of Human Immunodeficiency Virus Type 1," <u>Proc. Natl. Acad. Sci. USA</u> 90:6340-6344 (1993)
  - \* Zaug et al., "The *Tetrahymena* Ribozyme Acts Like an RNA Restriction Endonuclease," Nature 324:429-433 (1986)
  - Zhou et al., "Synthesis of Functional mRNA in Mammalian Cells by Bacteriophage T3 RNA Polymerase," <u>Mol. Cell. Biol.</u> 10:4529-4537 (1990)

\* Ziche et al., "Angiogenesis Can Be Stimulated or Represssed In vivo by a Change in GM3:GD3 Ganglioside Ratio" Lab. Invest. 67: 711-715 (1992)

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## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE (Case No. 02-325-A (400/047))

In the Application of:	Ologi	) \
Pavco et al.	0rī 2 1 2004 u	) 
Serial No.: 10/712,633	OCT 2 1 ZUUS Z	) Examiner: 1
•	The state of the s	) Group Art Unit: 1635
Filing Date: November 13,	2003	) )
		) Confirmation No. 6362
For: Nucleic Acid Based	Modulation of Female	)

Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450

Sir:

## TRANSMITTAL LETTER

In regard to the above identified application:

- 1. We are transmitting herewith the attached papers for the above identified new patent application:
  - Information Disclosure Statement;

**Reproductive Diseases and Conditions** 

- Information Disclosure Statement (IDS) PTO-1449 Form;
- Copies of IDS Citations for S/N 10/712,633 (Total 25 foreign patents and 103 other documents): and
- Return Receipt Postcard.
- 2. With respect to additional fees, no additional fee is required.
- 3. GENERAL AUTHORIZATION: Please charge any additional fees or credit overpayment to Deposit Account No. 13-2490. A duplicate copy of this sheet is enclosed.
- 4. CERTIFICATE OF MAILING UNDER 37 CFR § 1.8: The undersigned hereby certifies that this Transmittal Letter and the paper, as described in paragraph 1 hereinabove, are being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450 on \_\_\_\_\_\_\_\_ 2004.

Rv ·

Christopher

Reg. No. 48.701

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FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
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OTT :	INFORMATION DISCLOSURE STATEMENT BY APPLICANT  (Use several sheets if necessary)		
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OCT 2 1 2000 E		Pavco et al.	
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		November 13, 2003	

## **U.S. PATENT APPLICATION DOCUMENTS**

Examiner Initial		Document Number	Date	Name	Class	Subclass	Publication Date if Appropriate
	*	08/584,040	01/11/96	Pavco et al.			
	*	08/878,640	07/19/97	Usman et al.			
	*	09/205,520	12/03/98	Sullenger et al.			
	*	09/301,511	04/28/99	Beigelman et al.			
	*	09/371,772	08/10/99	Pavco et al.			
	*	09/476,387	12/30/99	Beigelman et al.			
	*	09/708,690	11/07/00	Pavco et al.			
	*	09/870,161	05/29/01	Pavco et al.			
	*	09/877,526	06/08/01	Usman et al.			
	*	09/918,728	07/31/01	Beigelman et al.			
	*	10/138,674	05/03/02	Pavco et al.			
	*	60/005,974	10/26/95	Pavco et al.			
	*	60/082,404	04/20/98	Thomspon et al.			
	*	60/101,174	09/21/98	Hartmann et al.			
	*	60/334,461	11/30/01	Sandberg et al.			

## **U.S. PATENT DOCUMENTS**

EXAMINER	DATE CONSIDERED

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
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Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
	*	4,987,071	01/22/91	Cech et al.			
	*	5,270,163	12/14/93	Gold et al.			
	*	5,334,711	08/02/94	Sproat et al.			
	*	5,475,096	12/12/95	Gold et al.			
	*	5,525,468	06/11/96	McSwiggen et al.			
	*	5,589,332	12/31/96	Shih et al.			
	*	5,624,803	04/29/97	Noonberg et al.			
	*	5,631,359	05/20/97	Chowrira et al.			
	*	5,670,633	09/23/97	Cook et al.			
	*	5,627,053	05/06/97	Usman et al.			
	*	5,672,695	09/30/97	Eckstein et al.	, <u></u>		
	*	5,716,824	02/10/98	Beigelman et al.			
	*	5,741,679	04/21/98	George et al.			
	*	5,792,847	08/11/98	Buhr et al.			
	*	5,807,718	09/15/98	Joyce et al.			
	*	5,834,186	11/10/98	George et al.			
	*	5,849,902	12/15/98	Arrow et al.			

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				Filing Date	э:	Group:	
		November	13, 2003				
*	5,854,038	12/29/98	Sullenger and Cech		<u> </u>		
*	5,871,914	02/16/99	Nathan et al.		-		
*	5,898,031	04/27/99	Crooke				
*	5,989,912	11/23/99	Arrow et al.				
*	6,001,311	12/14/99	Brennan				
*	6,005,087	12/21/99	Cook et al.				
*	6,107,094	08/22/00	Crooke				
*	6,127,173	10/03/00	Eckstein et al.				
*	6,159,714	12/12/00	Usman et al.				
*	6,180,613	01/30/01	Kaplitt et al.				
*	6,300,074	10/09/01	Gold et al.				
*	6,346,398	02/12/02	Pavco et al.				
*	6,476,205	11/05/02	Buhr et al.				
*	6,566,127	05/20/03	Pavco et al.				
		FOREIGN I	PATENT DOCUMENTS				
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FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce	Atty. Docket No.	Serial No.
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	*	360257	03/28/90	EP (Hampel et al.)		
	*	89/02439	03/23/89	WO (Arnold et al.)		
	*	91/03162	03/21/91	WO (Rossi et al.)		
	*	92/07065	09/23/91	WO (Eckstein et al.)		
	*	93/15187	08/05/93	WO (Usman et al.)		
	*	93/23057	11/25/93	WO (Thompson et al.)		
	1.	93/23569	11/25/93	WO (Draper et al.)		
	*	94/02595	02/03/94	WO (Sullivan et al.)		
	*	95/04142	02/09/95	WO (Robinson)		
	*	95/04818	02/16/95	WO (Draper et al.)		
	*	95/06731	03/09/95	WO (Usman et al.)		
	*	95/11304	Ck date	WO (Usman et al.)		
	*	95/11910	05/04/95	WO (Dudycz et al.)		
	*	95/13380	05/18/95	WO (Draper et al.)		
	*	95/21868	08/17/95	WO (Rockwell et al.)		-
	*	95/23225	08/31/95	WO (Stinchcomb et al.)		
	*	96/10390	04/11/96	WO (Asnell et al.)		
	*	96/10391	04/11/96	WO (Holland et al.)	 	

EXAMINER	DATE CONSIDERED

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FORM PTO-1449 (Rev. 2-32)			epartment of Commerce nt and Trademark Office	Atty. Docket No. 02-325-A (400/047)	<b>Serial No.</b> 10/712,633
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				Pavco et al.	
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*	96/10392	04/11/96	WO (Choi et al.)		
2.	96/18736	06/20/96	WO (Beigelman et al.)		
*	96/22689	08/01/96	WO (Pyle et al.)		
3.	97/15662	05/01/97	WO (Pavco et al.)		
*	97/26270	07/04/97	WO (Wincott et al.)		
*	98/13526	04/02/98	WO (Woolf et al.)		
*	98/27104	06/25/98	WO (Breaker et al.)		
*	98/28317	07/02/98	WO (Karpeisky et al.)		
4.	98/43993	03/30/98	WO (Breaker et al.)		
*	98/58058	12/23/98	WO (Ludwig et al.)		
5.	99/04819	02/04/99	WO (Klimuk et al.)		
6.	99/05094	02/04/99	WO (Beigelman et al.)		
7.	99/07409	02/18/99	WO (Deschamps de Paillette et al.)		
8.	99/14226	09/14/98	WO (Wengel et al.)		
*	99/16871	04/08/99	WO (Eckstein et al.)		
9.	99/32619	07/01/99	WO (Fire et al.)		
10.	99/49029	09/30/99	WO (Graham et al.)		
11.	99/53050	10/21/99	WO (Waterhouse et al.)		
12.	99/54459	10/28/99	WO (Thompson et al.)		

EXAMINER	DATE CONSIDERED

FORM PTO-14 (Rev. 2-32)	449			U.S. Department of Commerce Patent and Trademark Office		et No.	Serial No	) <b>.</b>
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	*	99/55857	11/04/99	WO (Beigelman et al.)				

*	99/55857	11/04/99	WO (Beigelman et al.)			
13.	99/61631	12/02/99	WO (Heifetz et al.)			
14.	99/63116	12/09/99	WO (Storella et al.)			
15.	00/01846	01/13/00	WO (Plaetinck et al.)	-		
*	00/24931	05/04/00	WO (Nathan et al.)			
*	00/26226	05/11/00	WO (Breaker et al.)			<u> </u>
16.	00/44895	08/03/00	WO (Kreutzer et al.)			
17.	00/44914	08/03/00	WO (Li et al.)			
18.	00/63364	10/26/00	WO (Pachuk et al.)			
19.	00/66604	05/04/00	WO (Wengel et al.)			
20.	00/73416	12/07/00	WO (Labarbera et al.)			
21.	01/29058	04/26/01	WO (Mello and Fire)			
22	01/32920	05/10/01	WO (Pappa)			<del></del> -
23.	01/36646	05/25/01	WO (Zernicka-Goetz et al.)			
24.	01/75164	10/11/01	WO (Tuschl et al.)			
25.	02/096927 (PCT/US02/17674)	12/05/02	Escobedo			

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc).

*	Aiello et al., "Suppression of Retinal Neovascularization in vivo by Inhibition of Vascula	ar
	Endothelial Growth Factor (VEGF) Using Soluble VEGF-Receptor Chimeric Proteins,"	

EXAMINER	DATE CONSIDERED

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office		Serial No.
(1107. 2-02)	r atent and Trademark Onice	02-325-A (400/047)	10/712,633
INFORMATION D STATEMENT BY			
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		Applicant:	
		Pavco et al.	
		Filing Date:	Group:
		November 13, 2003	

	<u>Proc. Natl. Acad. Sci. USA</u> 92: 10457-10461 (1995)
*	Aiello, et al., "Vascular Endothelial Growth Factor in Ocular Fluid of Patients with
	Diabetic Retinopathy and Other Retinal Disorders," 1994 New Engl. J. Med. 331, 1480
*	Akhtar and Juliano, "Cellular Uptake and Intracellular Fate of AntiSense
	Oligonucleotides," Trends Cell Biol. 2:139-144 (1992)
26.	The state of the s
	cultured neurons when coupled to a retro-inverso delivery peptide. The antisense
	activity depresses the target mRNA and protein in magnocellular oxytocin neurons,"
	Nucleic Acids Research 26:4910-4916 (1998)
27.	Bahramian et al., "Transcriptional and Posttranscriptional Silencing of Rodent a1(I)
	Collagen by a Homologous Transcriptionally Self-Silenced Transgene," Molecular and
	Cellular Biology, 274-283 (1999)
*	Bartel and Szostak, "Isolation of New Ribozymes From a Large Pool of Random
	Sequences," <u>Science</u> 261:1411-1418 (1993)
28.	Bass, "The short answer," Nature 411:428-429 (2001)
*	Beaucage and Iyer, "The Functionalization of Oligonucleotides Via Phosphoramidite
	Derivatives," Tetrahedron 49:1925-1963 (1993)
29.	Beaudry and Joyce, "Directed Evolution of an RNA Enzyme," Science 257:635-641
	(1992)
*	Beigelman et al., "Chemical Modification of Hammerhead Ribozymes," J. Biol. Chem.
	270:25702-25708 (1995)
30.	Bellon et al., "Amino-Linked Ribozymes: Post-Synthetic Conjugation of Half-
	Ribozymes," Nucleosides & Nucleotides 16:951-954 (1997)
31.	
	Iterative Solid Phase Synthesis," Bioconjugate Chem. 8:204-212 (1997)
32.	
	elements of the hairpin ribozyme," EMBO J. 12:2567-2574 (1993)

EXAMINER	DATE CONSIDERED

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
(Nev. 2-32)	ratent and Trademark Office	02-325-A (400/047)	10/712,633
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(Use	several sheets if necessary)		
		Applicant:	
		Pavco et al.	
		Filing Date:	Group:
		November 13, 2003	

	33.	Blesch, "Delivery of Neurotrophic Factors to Neuronal Targets: Toward Gene Therapy in the CNS." Drug News & Perspectives 13:360, 380 (2000)
		in the CNS," Drug News & Perspectives 13:269-280 (2000)
	34.	Boado et al., "Drug Delivery of Antisense Molecules to the Brain for Treatment of
		Alzheimer's Disease and Cerebral AIDS," Journal of Pharmaceutical Sciences
		87:1308-1315 (1998)
	0.5	
	35.	Boado, "Antisense drug delivery through the blood-brain barrier," Advanced Drug
		Delivery Reviews 15:73-107 (1995)
	*	Breaker and Joyce, "Inventing and improving ribozyme function: rational design versus
	*	iterative selection methods," <u>TIBTECH</u> 12:268-275 (1994)
	*	Breaker et al., "A DNA enzyme with Mg²-dependent RNA phosphoesterase activity,"
		Chemistry & Biology 2(10):655-660 (1995)
	*	Breaker, "Are engineered proteins getting competition from RNA?" Current Opinion in
		Biotechnology 7:442-448 (1996)
	36.	Breaker, "Catalytic DNA: in training and seeking employment," Nature Biotechnology
		17:422-423 (1999)
	37.	Brennan et al., "Two-Dimensional Parallel Array Technology as a New Approach to
		Automated Combinatorial Solid-Phase Organic Synthesis," Biotechnology and
		Bioengineering (Combinatorial Chemistry) 61:33-45 (1998)
	38.	Brody and Gold, "Aptamers as therapeutic and diagnostic agents," Reviews in
		Molecular Biotechnology 74:5-13 (2000)
	39.	Brogniez et al., "Fluorescence of Experimented Endometriosis in Rabbits, Using
	00.	
		Tamoxifen-eosin Association," <u>Human Reproduction</u> 10:927-931 (1995)
	*	Burger et al., "Experimental Corneal Neovascularization: Biomicroscopic, Angiographic,
		and Morphologic Correlation," Cornea 4:35-41 (1985/1986)
	*	Burgin et al., "Chemically Modified Hammerhead Ribozymes with Improved Catalytic
		Potos " Piochamistry 25:14000 14007 (4006) (valures as a sistely at 11 to 1 and 1
Ł		Rates," Biochemistry 35:14090-14097 (1996) (volume no mistakenly listed as 6)

EXAMINER	DATE CONSIDERED

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
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INFORMATION DISCL STATEMENT BY APP			
(Use several sheets if ne	ecessary)		
		Applicant:	
		Pavco et al.	
		Filing Date:	Group:
		November 13, 2003	

40. Burlina et al., "Chemical Engineering of RNase Resistant and Catalytically Active Hammerhead Ribozymes," <i>Bioorganic &amp; Medicinal Chemistry</i> 5:1999-2010 (1990)  * Caruthers et al., "Chemical Synthesis of Deoxyoligonucleotides and	
* Caruthers et al., "Chemical Synthesis of Deoxyoligonucleotides and	97)
Deoxyoligonucleotide Analogs," Methods in Enzymology 211:3-19 (1992)	
* Cech, "Ribozymes and Their Medical Implications," JAMA 260:3030-3034 (1988)	
<ul> <li>* Chartrand et al., "An oligodeoxyribonucleotide that supports catalytic activity in t</li> </ul>	he
hammerhead ribozyme domain," Nucleic Acids Research 23(20):4092-4096 (19	95)
* Chen et al., "Multitarget-Ribozyme Directed to Cleave at up to Nine Highly Cons	erved
HIV-1 env RNA Regions Inhibits HIV-1 Replication-Potential Effectiveness Agai	nst
Most Presently Sequenced HIV-1 Isolates," Nucleic Acids Research 20:4581-45	589
(1992)	
* Chowrira et al., "In Vitro and in Vivo Comparison of Hammerhead, Hairpin, and	
Hepatitis Delta Virus Self-Processing Ribozyme Cassettes," J. Biol. Chem. 269:	25856-
25864 (1994)	
* Christoffersen and Marr, "Riobozymes as Human Therapeutic Agents," J. Med.	Chem.
38:2023-2037 (1995) (also referred to as Christofferson and Marr)	
41. Christoffersen et al., "Application of computational techologies to ribozyme	
biotechnology products," <u>Journal of Molecular Structure (Theochem)</u> 311:273-2	84
(1994) (maybe referred to as Christofferson)	
* Cload and Schepartz, "Polyether Tethered Oligonucleotide Probes," J. Am. Che	m. Soc.
113:6324-6326 (1991)	
<ul> <li>Collins and Olive, "Reaction Conditions and Kinetics of Self-Cleavage of a Ribo</li> </ul>	zyme
Derived From Neurospora VS RNA," Biochemistry 32:2795-2799 (1993)	
42. Couture and Stinchcomb, "Anti-gene therapy: the use of ribozymes to inhibit ge	ne
function," <u>Trends In Genetics</u> 12:510-515 (1996)	
43. Crooke, "Advances in Understanding the Pharmacological Properties of Antiser	ise
Oligonucleotides," Advances in Pharmacology 40:1-49 (1997)	

EXAMINER	DATE CONSIDERED

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
(1101. 2 02)		02-325-A (400/047)	10/712,633
INFORMATION DISCL STATEMENT BY APP	LICANT		
(Use several sheets if no	necessary)		
		Applicant:	
		Pavco et al.	
		Filing Date:	Group:
		November 13, 2003	

	44.	Crooke, "Antisense Therapeutics," Biotechnology and Genetic Engineering Reviews
		15:121-157 (1998)
	45.	Crooke, "Progress in Antisense Technology: The End of the Beginning," Methods in
		Enzymology 313:3-45 (1999)
	46.	Cummings and Metcalf, "Effect of Surgically Induced Endometriosis on Pregnancy and
1		Effect of Pregnancy and Lactation on Endometriosis in Mice <sup>1</sup> " P.S.E.B.M. 212:332-337
		(1996)
	47.	Cummings et al., "Promotion of Endometriosis by 2,3, 7, 8-Tetrachlorodibenzo-p-dioxin
		in Rats and Mice: Time-Dose Dependence and Species Comparison 1,2" Toxicology and
		Applied Pharmacology 138:131-139 (1996)
	48.	D'Hooghe et al., "The Cycle Pregnancy Rate is Normal in Baboons with Stage I
		Endometriosis but Decreased in Primates with Stage II and Stage III-IV Disease,"
		Fertility and Sterility 66:809-813 (1996)
	49.	Delihas et al., "Natural antisense RNA/target RNA interactions: Possible models for
		antisense oligonucleotide drug design," Nature Biotechnology 15:751-753 (1997)
	*	Detmar et al., "Overexpression of Vascular Permeability Factor/Vascular Endothelial
		Growth Factor and its Receptors in Psoriasisi," 1994 J. Exp. Med. 180, 1141
	50.	Donnez et al., "Vascular Endothelial Growth Factor (VEGF) in Endometriosis," Human
		Reproduction 13:1686-1690 (1998)
	*	Dreyfus, "Restriction Ribozymes?" Einstein Quarterly Journal of Biology and Medicine
		6:92-93 (1988)
	*	Dropulic et al., "Functional Characterization of a U5 Ribozyme: Intracellular
		Suppression of Human Immunodeficiency Virus Type I Expression," Journal of Virology
		66:1432-1441 (1992)
	*	Durand et al., "Circular Dichroism Studies of an Oligodeoxyribonucleotide Containing a
		Hairpin Loop Made of a Hexaethylene Glycol Chain: Conformation and Stability,"
		Nucleic Acids Research 18:6353-6359 (1990)

EXAMINER	DATE CONSIDERED

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
	02-325-A (400/047)	10/712,633	
INFORMATION DISCL STATEMENT BY APP			
(Use several sheets if ne	ecessary)		
		Applicant:	
		Pavco et al.	
		Filing Date:	Group:
		November 13, 2003	

*	Duval-Valentin, "Specific inhibition of transcription by triple helix-forming
	oligonucleotides," Proc. Natl. Acad. Sci. USA 89:504-508 (1992)
51	Earnshaw et al., "Modified Oligoribonucleotides as Site-Specific Probes of RNA
	Structure and Function," Biopolymers 48:39-55 (1998)
*	Egholm et al., "PNA hybridizes to complementary oligonucleotides obeying the
	Watson-Crick hydrogen-bonding rules," Nature 365:566-568 (1993)
52	
	mammalian cells," Nature 411:494-498 (2001)
53.	Elkins and Rossi, "Ch. 2 - Cellular Delivery of Ribozymes," in Delivery Strategies for
	Antisense Oligonucleotide Therapeutics, edited by Akhtar, CRC Press, pp. 17-220
	(1995)
*	Elroy-Stein and Moss, "Cytoplasmic Expression System Based on Constitutive
i	Synthesis of Bacteriophage T7 RNA Polymerase in Mammalian Cells," Proc. Natl.
	Acad. Sci. USA 87:6743-6747 (1990)
54.	Genbank Accession no. X51602
55.	Emerich et al., "Biocompatability of Poly (DL-Lactide-co-Glycolide) Microshperes
	Implanted Into the Brain," Cell Transplantation 8:47-58 (1999)
56.	
	Interleukin-8 in Ovarian Endometriomata," Molecular Human Reproduction 6:50-54
	(2000)
*	Fava et al., "Vascular Permeability Factor/Endothelial Growth Factor (VPF/VEGF):
	Accumulation and Expression in Human Synovial Fluids and Rheumatoid Synovial
	Tissue," 1994 J. Exp. Med. 180, 341
*	Feldstein et al., "Two sequences participating in the autolytic processing of satellite
	tobacco ringspot virus complementary RNA," Gene 82:53-61 (1989)
*	Ferentz and Verdine, "Disulfied Cross-Linked Oligonucleotides," J. Am. Chem. Soc.
	113:4000-4002 (1991)

EXAMINER	DATE CONSIDERED

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
(1164. 2-32)	ratem and Trademark Office	02-325-A (400/047)	10/712,633
INFORMATION DISCL STATEMENT BY APP			
(Use several sheets if ne	ecessary)	Applicant:	
		Pavco et al.	
		Filing Date:	Group:
		November 13, 2003	

*	Ferrara, "Vascular Endothelial Growth Factor," 1993 Trends Cardiovas. Med. 3, 2244
57.	Fire et al., "Potent and Specific Genetic Interference by Double-Stranded RNA in
	Caenorhabditis Elegans," Nature 391:806-811(1998)
*	Folkman and Shing, "Angiogenesis," <u>J. Biol. Chem.</u> 267:10931-10934 (1992)
58.	Folkman et al., "Long-term Culture of Capillary Endothelial Cells," Proc. Natl. Acad. Sci.
*	<u>USA</u> 76:5217-5221 (1979)
	Folkman, "What is the Evidence that Tumors are Angiogenesis Dependent?" <u>Journal of</u> the National Cancer Institute 82:4-6 (1990)
*	Folkman, "Tumor Agniogenesis" 1985 Adv. Cancer. Res. 43, 175
*	Fong et al., "Role of the Flt-1 Receptor Tyrosine Kinase in Regulating the Assembly of Vascular Endothelium," 1995 Nature 376, 66 Corrected from specification
*	Forster and Altman, "External Guide Sequences for an RNA Enzyme," <u>Science</u> 249:783-786 (1990)
59.	Fox, "Targeting DNA with Triplexes," Current Medicinal Chemistry 7:17-37 (2000)
*	Freier et al., "Improved free-energy parameters for predictions of RNA duplex stability,"
	Proc. Natl. Acad. Sci. USA 83:9373-9377 (1986) [sometimes referred to as Frier]
*	Gao and Huang, "Cytoplasmic Expression of a Reporter Gene by Co-Delivery of T7 RNA Polymerase and T7 Promoter Sequence with Cationic Liposomes," <u>Nucleic Acids</u> Research 21:2867-2872 (1993)
60.	Genbank Accession No. NM 002019
61.	Genbank Accession No. NM 002253
62.	Genbank Accession No. NM 003376
*	Gitay-Goren et al., "The Binding of Vascular Endothelial Growth Factor to Its Receptos
	is Dependent on Cell Surface-associated Heparin-like Molecules," 1992 J. Biol. Chem. 267, 6093
*	Gold et al., Diversity of Oligonucleotide Functions," <u>Annu. Rev. Biochem.</u> 64:763-797 (1995)

EXAMINER	DATE CONSIDERED

	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
(NGV. 2-32)	ratent and Frademark Office	02-325-A (400/047)	10/712,633
INFORMATION DISCL STATEMENT BY APP			
(Use several sheets if no	ecessary)		
		Applicant:	;
		Pavco et al.	
		Filing Date:	Group:
		November 13, 2003	

63.	Gold, "Axonal Regeneration of Sensory Nerves is Delayed by Continuous Intrathecal
	Infusion of Nerve Growth Factor," Neuroscience 76:1153-1158 (1997)
64.	Good et al., "Expression of small, therapuetic RNAs in human nuclei," Gene Therapy 4:45-54 (1997)
*	Grant et al., "Insulin-like growth factor I acts as an angiogenic agent in rabbit cornea and retina: comparative studies with basic fibroblast growth factor," <i>Diabetologia</i> 36:282-291 (1993)
*	Griffin et al., "Group II intron ribozymes that cleave DNA and RNA linkages with similar efficiency, and lack contacts with substrate 2'-hydroxyl groups," <a href="#">Chemistry &amp; Biology 2:761-770 (1995)</a>
65.	Groothuis and Levy, "The entry of antiviral and antiretroviral drugs into the central nervous system," <u>Journal of NeuroVirology</u> 3:387-400 (1997)
*	Guerrier-Takada et al., "The RNA Moiety of Ribonuclease P Is the Catalytic Subunit of the Enzyme," Cell 35:849-857 (1983)
66.	Guo and Collins, "Efficent <i>trans</i> -cleavage of a stem-loop RNA substrate by a ribozyme derived from <i>Neurospora</i> VS RNA," <u>EMBO J.</u> 14:368-376 (1995)
67	Hagihara et al., "Widespread gene transfection into the central nervous system of primates," Gene Therapy 7:759-763 (2000)
68.	Hamilton, et al., "A Species of Small Antisense RNA in Posttranscriptional Gene Silencing in Plants," <i>Science</i> , 286, 950-952 (1999)
69.	Hammann et al., "Length Variation of Helix III in a Hammerhead Ribozyme and Its Influence on Cleavage Activity," <i>Antisense &amp; Nucleic Acid Drug Development</i> 9:25-31 (1999)
*	Hampel and Tritz, "RNA Catalytic Properties of the Minimum (-)sTRSV Sequence," Biochemistry 28:4929-4933 (1989)
*	Hampel et al., "'Hairpin' Catalytic RNA Model: Evidence for Helices and Sequence Requirement for Substrate RNA," <u>Nucleic Acids Research</u> 18:299-304 (1990)

EXAMINER	DATE CONSIDERED

	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
(NGV. 2-32)	(Nev. 2-32) Fatent and Trademark Office	02-325-A (400/047)	10/712,633
INFORMATION DISCL STATEMENT BY APP			
(Use several sheets if ne	ecessary)		
		Applicant:	
		Pavco et al.	
		Filing Date:	Group:
		November 13, 2003	

_		
	*	Haseloff and Gerlach, "Sequences required for self-catalysed cleavage of the satellite
L		RNA of tobacco ringspot virus," Gene 82:43-52 (1989)
	*	Haseloff and Gerlach, "Simple RNA Enzymes with New and Highly Specific
		Endoribonuclease Activities," Nature 334:585-591 (1988)
	70.	Hermann and Patel, "Adaptive Recognition by Nucleic Acid Aptamers," Science
		287:820-825 (2000)
	71.	Herrlinger et al., "HSV-1 Vectors for Gene Therapy of Experimental CNS Tumors,"
		Methods Mol. Med. 35:287-312 (2000)
	*	Hertel et al., "Numbering System for the Hammerhead," Nucleic Acids Research
		20:3252 (1992)
	72.	Ho et al., "Antisense Oligonucleotides for Target Validation in the CNS," Current
	'	Opinion in Molecular Therapeutics 1:336-343 (1999)
	73.	
	/3.	Hunziker et al., "Nucleic Acid Analogues: Synthesis and Properties, in Modern
	*	Synthetic Methods," VCH, 331-417 (1995)
	•	Ishiwata et al., "Physical-Chemistry Characteristics and Biodistribution of Poly(ethylene
		glycol)-Coated Liposomes Using Poly(oxyethylene) Cholesteryl Ether," Chem. Pharm.
		Bull. 43:1005-1011 (1995) (mistakenly referred to as Ishiwataet)
	*	Ishizaka et al., "Isolation of Active Ribozymes from an RNA Pool of Random
		Sequences Using an Anchored Substrate RNA," Biochemical and Biophysical
L		Research Communication 214(2):403-409 (1995)
	*	Izant and Weintraub, "Constitutive and Conditional Suppression of Exogenous and
		Endogeneous Genes by Anti-Sense RNA," Science 229:345-352 (1985)
	*	Jaeger et al., "Improved Predictions of Secondary Structures for RNA," Proc. Natl.
		Acad. Sci. USA 86:7706-7710 (1989)
	74.	Jarvis et al., "Optimizing the Cell Efficacy of Synthetic Ribozymes," Journal of
		Biological Chemistry 271:29107-29112 (1996)
	*	Jaschke et al., "Automated Incorporation of Polyethylene Glycol into Synthetic
ــــــــــــــــــــــــــــــــــــــ		readonite of any reacondated moorporation of religions of the organization of the orga

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	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
(NGV. 2-32)	Rev. 2-32) Patent and Trademark Office	02-325-A (400/047)	10/712,633
INFORMATION DISCL STATEMENT BY APP			
(Use several sheets if no	ecessary)		
		Applicant:	
		Pavco et al.	
		Filing Date:	Group:
		November 13, 2003	

	Oligonucleotides," <u>Tetrahedron Letters</u> 34:301-304 (1993)	
75.	Jayasena, "Aptamers: An Emerging Class of Molecules that Rival Antibodies in	
	Diagnostics," Clinical Chemistry 45:1628-1650 (1999)	
*	Jeffries and Symons, "A Catalytic 13-mer Ribozyme," Nucleic Acids Research 17:1371-	
	1377 (1989) (also referred to as Jefferies)	
*	Jellinek et al., "Inhibitions of Receptor Binding by High-Affinity RNA Ligands to Vascular	
	Endothelial Growth Factor," Biochemistry 33:10450-10456 (1994)	
 76.	Jolliet-Riant and Tillement, "Drug transfer across the blood-brain barrier and	
	improvement of brain delivery," Fundam. Clin. Pharmacol. 13:16-26 (1999)	
*	Joyce et al., "Amplification, mutation and selection of catalytic RNA," Gené 82:83-87	
	(1989)	
*	Joyce, "Directed Molecular Evolution," Scientific American 267:90-97 (1992)	
77.	Karpeisky et al, "Highly Efficient Synthesis of 2'-O-Amino Nucleosides And Their	
	Incorporation in Hammerhead Ribozymes," <u>Tetrahedron Letters</u> 39:1131-1134 (1998)	
 *	Kashani-Sabet et al., "Reversal of the Malignant Phenotype by an Anti-ras Ribozyme,"	
	Antisense Research & Development 2:3-15 (1992)	
*	Kim and Cech, "Three-dimensional model of the active site of the self-splicing rRNA	
	precursor of <i>Tetrahymena</i> ," Proc. Natl. Acad. Sci. USA 84:8788-8792 (1987)	
 *	Kim et al., "Inhibition of vascular endothelial growth factor-induced angiogenesis	
	suppresses tumour growth <i>in vivo</i> ," Nature 362:841-844 (1993)	
*	Koch et al., "Vascular Endothelial Growth Factor: A Cytokine Modulating Endothelial	
	Function in Rheumatoid Arthritis," 1994 <i>J. Immunol.</i> 152, 4149	
 *	Kore, et al., "Sequence specificity of the hammerhead ribozyme revisistsed; the NIH	
	rule", Nucleic Acids Research, 26(18):4116-4120 (1998).	
*	Kumar and Ellington, "Artificial evolution and natural ribozymes," FASEB J. 9:1183-	
	1195 (1995)	
 	1100 (1000)	

EXAMINER	DATE CONSIDERED

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
(Nev. 2-32) Fatent and Trademark	ratent and Industrial & Office	02-325-A (400/047)	10/712,633
INFORMATION DISCL STATEMENT BY APP			
(Use several sheets if ne	ecessary)		
		Applicant:	
		Pavco et al.	
		Filing Date:	Group:
		November 13, 2003	

78.	Kusser, "Chemically modified nucleic acid aptamers for in vitro selections: evolving evolution," <i>Reviews in Molecular Biotechnology</i> 74:27-38 (2000)
*	Lasic and Needham "The 'Stealth' Liposome: A Prototypical Biomaterial," Chemical Reviews 95:2601-2627 (1995)
79.	Lasic and Papahadjopoulos, "Liposomes Revisited," <u>Science</u> 267:1275-1276 (1995)
*	
	Lepri et al., "Effect of Low Molecular Weight Heparan Sulphate on Angiogenesis in the Rat Cornea after Chemical Cauterization," <i>Journal of Ocular Pharmacology</i> 10:273-281 (1994)
*	L'Huillier et al., "Cytoplasmic Delivery of Ribozymes Leads to Efficient Reduction in $\alpha$ -Lactalbumin mRNA Levels in C1271 Mouse," EMBO J. 11:4411-4418 (1992)
*	Li and Altman, "Cleavage by RNase P of gene N mRNA reduces bacteriophage λ burst size," Nucleic Acids Research 24:835-842 (1996)
*	Lieber et al., "Stable High-Level Gene Expression in Mammalian Cells by T7 Phage RNA Polymerase," Methods Enzymol. 217:47-66 (1993)
*	Limbach et al., "Summary: the modified nucleosides of RNA," <u>Nucleic Acids Research</u> 22(12):2183-2196 (1994)
80.	Lin and Matteucci, "A Cytosine Analogue Capable of Clamp-Like Binding to a Guanine in Helical Nucleic Acid," <i>J. Am. Chem. Soc.</i> 120:8531-8532 (1998)
81.	Lin et al., "Policing rogue genes," Nature, 402, 128-129 (1999)
*	Lisziewicz et al., "Inhibition of Human Immunodeficiency Virus Type 1 Replication by Regulated Expression of a Polymeric Tat Activation Response RNA Decoy as a Strategy for Gene Therapy in AIDS," Proc. Natl. Acad. Sci. U.S.A. 90:8000-8004 (1993)
*	Liu et al., "Cationic Liposome-mediated Intravenous Gene Delivery," J. Biol. Chem. 270(42):24864-24870 (1995)
*	Long and Uhlenbeck, "Kinetic characterization of intramolecular and intermolecular hammerhead RNAs with stem II deletions," <u>Proc. Natl. Acad. Sci. USA</u> 91:6977-6981 (1994)

EXAMINER	DATE CONSIDERED

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
(1.01. 2.02)		02-325-A (400/047)	10/712,633
INFORMATION DISCL STATEMENT BY APP			
(Use several sheets if n	ecessary)		
		Applicant:	
		Pavco et al.	
		Filing Date:	Group:
		November 13, 2003	

	*	Ma et al., "Design and Synthesis of RNA Miniduplexes via a Synthetic Linker
		Approach," <u>Biochemistry</u> 32:1751-1758 (1993)
	*	Ma et al., "Design and Synthesis of RNA Miniduplexes via a Synthetic Linker Approach.
1		2. Generation of Covalently Closed, Double-Stranded Cyclic HIV-1 TAR RNA Analogs
		with High Tat-Binding Affinity," Nucleic Acids Research 21:2585-2589 (1993)
	82.	Maher et al., "Kinetic Analysis of Oligodeoxyribonucleotide-Directed Triple-Helix
		Formation on DNA," <i>Biochemistry</i> 29:8820-8826 (1990)
	*	Mathews et al., "A Receptor Tyrosine Kinase cDNA Isolated from a Population of
		Enriched Primitive Hematopoiectic cells and Exhibiting Close Genetic Linkage to c-kit,"
		1991, <i>Proc. Natl. Acad. Sci.,</i> USA, 88, 9026
	*	McCurdy et al., "Deoxyoligonucleotides with Inverted Polarity: Synthesis and Use in
		Triple-Helix Formation" Nucleosides & Nucleotides 10:287-290 (1991)
	*	McGarry and Lindquist, "Inhibition of heat shock protein synthesis by heat-inducible
		antisense RNA," <u>Proc. Natl. Acad. Sci. USA</u> 83:399-403 (1986)
	83.	McLaren et al., "Vascular Endothelial Growth Factor (VEGF) Concentrations are
		Elevated in Peritoneal Fluid of Women with Endometriosis," Human Reproduction
		11:220-223 (1996)
	84.	McLaren et al., "Vascular Endothelial Growth Factor is Produced by Peritoneal Fluid
		Macrophages in Endometriosis and Is Regulated by Ovarian Steroids," <u>J. Clin. Invest.</u>
		98:482-489 (1996)
	85.	McLaren, "Vascular Endothelial Growth Factor and Endometriotic Angiogenesis,"
		Human Reproduction Update 6:45-55 (2000)
	86.	Mesmaeker et al, "Novel Backbone Replacements for Oligonucleotides," American
		Chemical Society, pp. 24-39 (1994)
	*	Michels and Pyle, "Conversion of a Group II Intron into a New Multiple-Turnover
		Ribozyme that Selectively Cleaves Oligonucleotides: Elucidation of Reaction
		Mechanism and Structure/Function Relationships," Biochemistry 34:2965-2977 (1995)

EXAMINER	DATE CONSIDERED

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
(1104. 2 02)		02-325-A (400/047)	10/712,633
INFORMATION DISCL STATEMENT BY APP			
(Use several sheets if ne	ecessary)		
		Applicant:	
		Pavco et al.	
		Filing Date:	Group:
		November 13, 2003	

	87.	Millauer et al., "Glioblastoma growth inhibited in vivo by a dominant-negative Flk-1
		mutant," Letters to Nature 367:576-579 (1994)
	*	Millauer, "High Affintiy VEGF Binding and Developmental Expression Suggest Flk-1 as
	<u> </u>	a Major Regulator of Vasculogenesis and Angiogenesis," Cell 72:835-846 (1993)
	*	Miller et al., "Vascular Endothelial Growth Factor/Vascular Permeability Factor is
		Temporally and Spatially Correlated with Ocular Angiogenesis in a Primate Model,"
		1994 Am. J. Pathol. 145, 574
1	88.	Milligan and Uhlenbeck, "Synthesis of Small RNAs Using T7 RNA Polymerase,"
		Methods Enzymol. 180:51-62 (1989)
	89.	Milner et al., "Selecting effective antisense reagents on combinatorial oligonucleotide
		arrays," Nature Biotechnology 15:537-541 (1997)
	90.	Moore and Sharp, "Site-Specific Modification of Pre-mRNA: The 2'-Hydroxyl Groups at
		the Splice Sites," <u>Science</u> 256:992-996 (1992)
	*	Mukhopadhyay et al., "Antisense Regulation of Oncogenes in Human Cancer," Critical
		Reviews in Oncogenesis 7:151-190 (1996)
	*	Nakamaye and Eckstein, "AUA-Cleaving Hammerhead Ribozymes: Attempted
<u> </u>		Selection for Improved Cleavage," Biochemistry 33:1271-1277 (1994
	*	Nathans and Smith, "Restriction Endonucleases in the Analysis and Restructuring of
	ļ	DNA Molecules," <u>Ann. Rev. Biochem.</u> 44:273-293 (1975)
	*	Neufeld et al., "Vascular Endothelial Growth Factor and Its Receptors," Progress in
		Growth Factor Research 5:89-97 (1994)
	91.	Noonberg et al., In vivo generation of highly abundant sequence-specific
		oligonucleotides for antisense and triplex gene regulation," Nucleic Acids Research
	ļ	22(14):2830-2836 (1994)
	*	Norrby, "Angiogenesis: new aspects relating to its initiation and control," APMIA
		105:417-437 (1997)
	*	Ohkawa et al., "Activities of HIV-RNA Targeted Ribozymes Transcribed From a 'Shot-

EXAMINER	DATE CONSIDERED

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
r dent and Trademark Office	02-325-A (400/047)	10/712,633	
INFORMATION DISCL STATEMENT BY APP			
(Use several sheets if ne	ecessary)		
		Applicant:	
		Pavco et al.	
		Filing Date:	Group:
		November 13, 2003	

	Gun' Type Ribozyme-trimming Plasmid," Nucleic Acids Symp. Ser. 27:15-16 (1992)
*	Ojwang et al., "Inhibition of Human Immunodeficiency Virus Type 1 Expression by a
	Hairpin Ribozyme," Proc. Natl. Acad. Sci. USA 89:10802-10806 (1992)
*	Oku et al., "Real-time analysis of liposomal trafficking in tumor-bearing mice by use of
	positron emission tomography," <u>Biochimica et Biophysica</u> Acta 1238:86-90 (1995)
*	Ono et al., "DNA Triplex Formation of Oligonucleotide Analogues Consisting of Linker
	Groups and Octamer Segments That Have Opposite Sugar-Phosphate Backbone
	Polarities," Biochemistry 30:9914-9921 (1991)
*	O'Reilly et al., "Angiostatin: A Novel Angiogenesis Inhibitor That Mediates the
	Suppression of Metastases by a Lewis Lung Carcinoma," Cell 79:315-328 (1994)
*	Orgel, "Selection in vitro," Proc. R. Soc. London B. 205:435-442 (1979)
*	Ormerod et al., "Effects of Altering the Eicosanoid Precursor Pool on
	Neovascularization and Inflammation in the Alkali-burned Rabbit Cornea," American
	Journal of Pathology 137:1243-1252 (1990)
*	Pandey et al., "Role ov B61, the Ligand for the Eck Receptor Tyrosine Kinase, in TNF-
	α-Induced Angiogenesis," Science 268:567-569 (1995)
92.	Pardridge et al., "Vector-mediated delivery of a polyamide ("peptide") nucleic acid
	analogue through the blood-brain barrier in vivo," Proc. Natl. Acad. Sci. USA 92:5592-
	5596 (1995)
*	Passaniti et al., "A Simple, Quantitative Method for Assessing Angiogenesis and
	Antiangiogenic Agents Using Reconstituted Basement Membrane, Heparin, and
	Fibroblast Growth Factor," Laboratory Investigation 67:519-528 (1992)
93.	Peel and Klein, "Adeno-associated virus vectors: activity and applications in the CNS,"
	Journal of Neuroscience Methods 98:95-104 (2000)
*	Perreault et al., "Mixed Deoxyribo- and Ribo-Oligonucleotides with Catalytic Activity,"
	Nature 344:565-567 (1990) (often mistakenly listed as Perrault)
*	Perrotta and Been, "Cleavage of Oligoribonucleotides by a Ribozyme Derived from the

EXAMINER	DATE CONSIDERED

	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
(NOV. 2-02)	ratent and Frademark Office	02-325-A (400/047)	10/712,633
INFORMATION DISCL STATEMENT BY APP			
(Use several sheets if no	ecessary)		
		Applicant:	
		Pavco et al.	
		Filing Date:	Group:
		November 13, 2003	

	Hepatitis δ Virus RNA Sequence," Biochemistry 31:16-21 (1992)
94.	Peterson et al., "Future Prospects of Gene Therapy for Treating CNS Diseases,"
	Central Nervous System Diseases Chapter 24:485-508 (2000)
*	Pieken et al., "Kinetic Characterization of Ribonuclease-Resistant 2'-Modified
	Hammerhead Ribozymes," Science 253:314-317 (1991)
95.	Pierce et al., "Regulation of Vascular Endothelial Growth Factor by Oxygen in a Model
	of Retinopathy of Prematurity," Arch Ophthalmol 114:1219-1228 (1996)
*	Pierce et al., "Vascular endothelial growth factor/vascular permeability factor
	expression in a mouse model of retinal neovascularization," Proc. Natl. Acad. Sci. USA
	92:905-909 (1995)
96.	Plate, "Vascular endothelial growth factor is potential tumor angiogenesis factor in
	human gilomas <i>in vivo</i> ," <u>Nature</u> 359:845-848 (1992)
97.	Player and Torrence, "The 2-5A System: Modulation of Viral and Cellular Processes
	Through Acceleration of RNA Degradation," Pharmacol Ther. 78:55-113 (1998)
*	Plouet et al., "Isolation and Characterization of a Newly Identified Endothelial Cell
 	Mitogen Produced by AtT-20 Cells," 1989 EMBO J. 8, 3801
98.	Praseuth et al., "Triple helix formation and the antigene for sequence-specific control of
	gene expression," Biochimica et Biophysica Acta 1489:181-206 (1999)
99.	Quereda et al., "Individual and Combined Effects of Triptoreline and Gestrinone on
	Experimental Endometriosis in Rats," European Obstetrics & Gynecology and
	Reproductive Biology 67:35-40 (1996)
*	Richardson and Schepartz, "Tethered Oligonucleotide Probes. A Strategy for the
 	Recognition of Structured RNA," J. Am. Chem. Soc. 113:5109-5111 (1991)
*	Robinson et al., "Oligodeozynucleotides Inhibit Retinal Neovascularization in a Murine
	Model of Proliferation Retinopathy," Proc. Natl. Acad. Sci. USA 93: 4851-4856 (1996)
*	Rossi et al., "Ribozymes as Anti-HIV-1 Therapeutic Agents: Principles, Applications,
	and Problems," Aids Research and Human Retroviruses 8:183-189 (1992)

EXAMINER	DATE CONSIDERED

	FORM PTO-1449  (Rev. 2-32)  U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
(NEV. 2-32)		02-325-A (400/047)	10/712,633
INFORMATION DISCL STATEMENT BY APP			
(Use several sheets if ne	ecessary)		
		Applicant:	
		Pavco et al.	
		Filing Date:	Group:
		November 13, 2003	

*	Santoro and Joyce, "A general purpose RNA-cleaving DNA enzyme," Proc. Natl. Acad.
	Sci. USA 94:4262-4266 (1997)
100.	Santoro et al., "Mechanism and Utility of an RNA-Cleaving DNA Enzyme," <i>Biochemistry</i> 37:13330-13342 (1998)
101.	Santoro et al., "RNA Cleavage by a DNA Enzyme with Extended Chemical Functionality," <i>J. Am. Chem. Soc.</i> 122:2433-2439 (2000)
*	Sarver et al., "Ribozymes as Potential Anti-HIV-1 Therapeutic Agents" <u>Science</u> 247:1222-1225 (1990)
*	Saville and Collins, "A Site-Specific Self-Cleavage Reaction Performed by a Novel RNA In Neurospora Mitochondria," Cell 61:685-696 (1990)
*	Saville and Collins, "RNA-Mediated Ligation of Self-Cleavage Products of a Neurospora Mitochondrial Plasmid Transcript," Proc. Natl. Acad. Sci. USA 88:8826-8830 (1991)
*	Scanlon et al., "Ribozyme-Mediated Cleavage of c-fos mRNA Reduces Gene Expression of DNA Synthesis Enzymes and Metallothionein," <a href="Proc. Natl. Acad. Sci.uSA 88:10591-10595">Proc. Natl. Acad. Sci.uSA 88:10591-10595</a> (1991)
*	Scaringe et al., "Chemical synthesis of biologically active oligoribonucleotides using β-cyanoethyl protected ribonucleoside phosphoramidites," <u>Nucl Acids Res.</u> 18:5433-5441 (1990)
102.	Schmajuk et al., "Antisense Oligonucleotides with Different Backbones," <i>The Journal of Biological Chemistry</i> 274:21783-21789 (1999)
103.	Schroeder et al., "Diffusion Enhancement of Drugs by Loaded Nanoparticles in Vitro," Prog. Neuro-Psychopharmacol. & Biol. Psychiat. 23:941-949 (1999) [sometimes cited by RPI as Prog Neuropsychopharmacol Biol Psychiatry 23:941-949, 1999]
*	Seela and Kaiser, "Oligodeoxyribonucleotides containing 1,3-propanediol as nucleoside substitute," Nucleic Acids Research 15:3113-3129 (1987)

EXAMINER	DATE CONSIDERED

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
(Nev. 2-32)	Fatent and Trademark Office	02-325-A (400/047)	10/712,633
INFORMATION DISCL STATEMENT BY APP			
(Use several sheets if ne	ecessary)		
		Applicant:	
		Pavco et al.	
		Filing Date:	Group:
		November 13, 2003	

*	Senger et al., "Vascular permeability factor (VPF, VEGF) in tumor biology," Cancer and Matastasis Reviews 12:303-324 (1993)
104.	
*	Shalaby et al., "Failure of Blood-island Formation and Vasculogenesis in Flk-1-deficient Mice," 1995 Nature 376, 62
106.	Sharkey et al., "Vascular Endothelial Growth Factor Expression in Human Endometrium is Regulated by Hypoxia," The Journal of Clinical Endocrinology & Metabolism 85:402-409 (2000)
107.	Sharp et al., "RNAi and double-strand RNA," Genes & Development, 13:139-141 (1999)
108.	Shibuya et al., "Nucleotide sequence and expression of a novel human receptor-type tyrosine kinase gene ( <i>flt</i> ) closely related to the <i>fms</i> family," Oncogene 5:519-524 (1990)
109.	Shifren et al., "Ovarian Steroid Regulation of Vascular Endothelial Growth Factor in the Human Endometrium: Implications for Angiogenesis during the Menstrual Cycle and in the Pathogenesis of Endometriosis," The Journal of Clinical Endocrinology & Metabolism 81:3112-3118 (1996)
*	Shweiki et al., "Patterns of Expression of Vascular Endothelial Growth Factor (VEGF) and VEGF Receptors in Mice Suggest a Role in Hormonally Regulated Angiogenesis," 1993 Clin. Invest. 91: 2235-2243
110.	Silverman et al., "Selective RNA Cleavage by Isolated RNase L Activated with 2-5A Antisense Chimeric Oligonucleotides," <i>Methods in Enzymology</i> 313:522-533 (1999)
*	Stein and Cheng, "Antisense Oligonucleotides as Therapeutic Agents - Is the Bullet Really Magical?" Science 261:1004-1288 (1993)
111.	

EXAMINER	DATE CONSIDERED

FORM PTO-1449  (Rev. 2-32)  U.S. Department of Commerce Patent and Trademark Office		Atty. Docket No.	Serial No.
	02-325-A (400/047)	10/712,633	
INFORMATION DISCL STATEMENT BY APP			
(Use several sheets if ne	ecessary)		
		Applicant:	
		Pavco et al.	
		Filing Date:	Group:
		November 13, 2003	

F	
112	Stoeckemann et al., "Effects of the Progesterone Antagonists Onapristone (ZK 98 299) and ZK 136 799 on Surgically Induced Endometriosis in Intact Rats," <u>Human</u>
	Reproduction 10:3264-3271 (1995)
113	Strauss, Evelyn, "Molecular Biology: Candidate 'Gene Silencers' Found," Molecular
	Biology, Vol. 286, No. 5441, p. 886 (1999) [sometimes mistakenly referred to as being
	published in Science]
114	
	Oligonucleotide-Directed Triple-Helix Formation," Science 249:73-75 (1990)
115	5
	Human Immunodeficiency Virus Replication," Cell 63:601-608 (1990)
116	
	Molecular Therapeutics 2:100-105 (2000)
*	Szostak and Ellington, "Ch. 20 - In Vitro Selection of Functional RNA Sequences," in
	The RNA World, edited by Gesteland and Atkins, Cold Spring Harbor Laboratory Press,
	pp. 511-533 (1993)
*	Szostak, "In Vitro Genes," TIBS 17:89-93 (1993)
*	Taira et al., "Construction of a novel RNA-transcript-trimming plasmid which can be
	used both in vitro in place of run-off and (G)-free transcriptions and in vivo as multi-
	sequences transcription vectors," Nucleic Acids Research 19:5125-5130 (1991)
*	Takahashi et al., "Markedly Increased Amounts of Messenger RNAs for Vascular
	Endothelial Growth Factor and Placenta Growth Factor in Renal Cell Carcinoma
	Associated with Angiogenesis," Cancer Research 54:4233-4237 (1994)
*	Takeshita et al., "Therapeutic Angiogenesis: A Single Intraarterial Blous of Vascular
	Endothelial Growth Factor Augments Revascularization in a Rabbit Ischemic Hind Limb
	Model," 1995 J. Clin. Invest. 93, 662 Corrected from Specification
*	Tang et al., "Examination of the catalytic fitness of the hammerhead ribozyme by in
	vitor selection," RNA 3:914-925 (1997)

EXAMINER	DATE CONSIDERED

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
(1011)		02-325-A (400/047)	10/712,633
INFORMATION DISCL STATEMENT BY APP			
(Use several sheets if ne	ecessary)		
		Applicant:	
		Pavco et al.	
		Filing Date:	Group:
		November 13, 2003	

*	T
	Terman et al., "Identification of a New Endothelial Cell Growth Factor Receptor
	Tyrosine Kinase," 1991 Oncogene 6, 1677
*	Thompson et al., "Improved accumulation and activity of ribozymes expressed from a
	tRNA-based RNA polymerase III promoter," <u>Nucleic Acids Research</u> 23:2259-2268
	(1995)
*	Torrence et al., "Targeting RNA for degradation with a (2'-5') oligoadenylate-antisense
	chimera," Proc. Natl. Acad. Sci. USA 90:1300-1304 (1993)
*	Turner et al., "Free Energy Increments for Hydrogen Bonds in Nucleic Acid Base
İ	Pairs," J. Am. Chem. Soc. 109:3783-3785 (1987)
*	Turner et al., "Improved Parameters for Prediction of RNA Structure," Cold Spring
	Harbor Symposia on Quantitative Biology Volume LII, pp. 123-133 (1987)
117.	Tuschl et al., "Targeted mRNA Degradation by Double-Stranded RNA In Vitro," Genes
	& Development 13:3191-3197 (1999)
118.	Tyler et al., "Peptide nucleic acids targeted to the neurotensin receptor and
	administered i.p. cross the blood-brain barrier and specifically reduce gene
	expression," <i>Proc. Natl. Acad. Sci. USA</i> 96:7053-7058 (1999)
119.	Tyler et al., "Specific gene blockade shows that peptide nucleic acids readily enter
	neuronal cells in vivo," FEBS Letters 421:280-284 (1998)
*	Uhlenbeck, "A Small Catalytic Oligoribonucleotide," Nature 328:596-600 (1987)
120.	Uhlmann and Peyman, "Antisense Oligonucleotides: A New Therapeutic Principle,"
	Chemical Reviews 90:544-584 (1990)
 *	Usman and Cedergren, "Exploiting the chemical synthesis of RNA," TIBS 17:334-339
	(1992) (Corrected from Specification)
*	Usman and McSwiggen, "Ch. 30 - Catalytic RNA (Ribozymes) as Drugs," Annual
	Reports in Medicinal Chemistry 30:285-294 (1995)
 *	Usman et al., "Automated Chemical Synthesis of Long Oligoribonucleotides Using 2'-O-
	Silylated Ribonucleoside 3'-O-Phosphoramidites on a Controlled-Pore Glass Support:
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EXAMINER	DATE CONSIDERED

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
(Nev. 2-32)	ratent and Trademark Office	02-325-A (400/047)	10/712,633
INFORMATION DISCL STATEMENT BY APP			
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		Applicant:	
		Pavco et al.	
		Filing Date:	Group:
		November 13, 2003	

	Synthesis of a 43-Nucleotide Sequence Similar to the 3'-Half Molecule of an
	Escherichia coli Formylmethoionine tRNA," J. Am. Chem. Soc. 109:7845-7854 (1987)
*	Usman et al., "Chemical modification of hammerhead ribozymes: activity and nuclease
	resistance," Nucleic Acids Syposium Series 31:163-164 (1994)
121	Usman et al., "Hammerhead ribozyme engineering," <u>Current Opinion in Structural</u> <u>Biology</u> 1:527-533(1996)
*	Vaish et al., "Isolation of Hammerhead Ribozymes with Altered Core Sequences by in Vitro Selection," <u>Biochemistry</u> 36:6495-6501 (1997)
*	Vaisman et al., "Characterization of the Receptors for Vascular Endothelial Growth," 1990 J. Biol. Chem. 265, 19461
*	Ventura et al., "Activation of HIV-Specific Ribozyme Activity by Self-Cleavage," <u>Nucleic Acids Research</u> 21:3249-3255 (1993)
122	Verma and Eckstein, "Modified Oligonucleotides: Synthesis and Strategy for Users," Annu. Rev. Biochem. 67:99-134 (1998)
123	Warashina, et al., "Extremely High and Specific Activity of DNA Enzymes in Cells with a Philadelphia Chromosome, Chemistry & Biology, 6(4):237-250 (1999)
124	
*	Weckbecker et al., 1992, Angiogenesis: Key principles-Science-Technology-Medicine, ed R. Steiner)
*	Weerasinghe et al., "Resistance to Human Immunodeficiency Virus Type 1 (HIV-1) Infection in Human CD4 <sup>+</sup> Lymphocyte-Derived Cell Lines Conferred by Using Retroviral Vectors Expressing an HIV-1 RNA-Specific Ribozyme," <u>Journal of Virology</u> 65:5531-5534 (1994)
125	Wellstein and Czubayko, "Inhibition of Fibroblast Growth Factors," <u>Breast Cancer</u> <u>Research and Treatment</u> 38:109-119 (1996)

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		November 13, 2003	

*	Ziche et al., "Angiogenesis Can Be Stimulated or Represssed In vivo by a Change in GM3:GD3 Ganglioside Ratio" 1992 Lab. Invest. 67: 711-715
*	Zhou et al., "Synthesis of Functional mRNA in Mammalian Cells by Bacteriophage T3 RNA Polymerase," Mol. Cell. Biol. 10:4529-4537 (1990)
*	Zaug et al., "The <i>Tetrahymena</i> Ribozyme Acts Like an RNA Restriction Endonuclease," Nature 324:429-433 (1986)
*	Yu et al., "A Hairpin Ribozyme Inhibits Expression of Diverse Strains of Human Immunodeficiency Virus Type 1," Proc. Natl. Acad. Sci. USA 90:6340-6344 (1993)
129.	Wu-Pong, "Oligonucleotides: Opportunities for Drug Therapy and Research," <u>BioPharm</u> pp20-33 (1994)
 128.	Woolf et al., "Specificity of Antisense Oligonucleotides <i>in vivo</i> ," <u>Proc. Natl. Acad. Sci. USA</u> 89:7305-7309 (1992)
127.	Wincott et al., "A Practical Method for the Production of RNA and Ribozymes,"  Methods in Molecular Biology 74:59-69 (1997)
*	Wincott et al., "Synthesis, deprotection, analysis and purification of RNA and ribozymes," <u>Nucleic Acids Research</u> 23(14):2677-2684 (1995)
126.	Werner and Uhlenbeck, "The effect of base mismatches in the substrate recognition helices of hammerhead ribozymes on binding and catalysis," <u>Nucleic Acids Research</u> 23:2092-2096 (1995)

EXAMINER	DATE CONSIDERED



Hon. Commissioner of

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Patents and Trademarks

Re: Pavco, et al.

Case No.: 02-325-A (400/047)

## Nucleic Acid Based Modulation of Female Reproductive Diseases and Conditions

Sir:

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Respectfully,

McDonnell Boehnen Hulbert & Berghoff
Attorney for Applicant